

Keynote Address Program

100 How Severe Is Autism - Really?

This session reviews the coexisting problems that usually exist in individuals with a diagnosis of autism spectrum disorder. It concludes on the note that it is possibly these associated problems and disorders that often drive the poor outcome that so many people now almost take for granted will be a consequence of autism in the longer term perspective. Language disorders, intellectual developmental disorders, non-verbal learning disability, epilepsy, medical disorders such as tuberous sclerosis and fragile X syndrome, ADHD, and depression are often the "real" cause of negative outcome in autism. Many people in the general population have marked autistic features without major "lifetime impairment". The focus on *autism only* in early intervention programs is most likely a mistake.

100.001 How Severe is Autism - Really?. C. Gillberg*,
Gillberg Neuropsychiatry Centre, University of Gothenburg

101 Understanding the Scientific, Ethical and Social Challenges in Autism Biomarker Research

Moderator: P. Ashwood The M.I.N.D. Institute, University of California, Davis

Organizer: L. Hewitson The Johnson Center for Child Health and Development

While the development of a blood biomarker as a screening or diagnostic tool for autism spectrum disorders is of great interest to the scientific and medical communities, it is also attracting intense scrutiny from other stakeholders including people with autism, ethicists, and parents. This symposium will therefore address the scientific, ethical and social challenges associated with the development of biomarkers for autism, and provide an update on the current status of research in this field. We will describe how the heterogeneity of autism, gender bias, and potential comorbidities, could derail the promise of identifying objective, reliable, and universally accepted biomarkers. We will consider the ethical and social issues relating to the development of biomarkers for autism in order to identify and describe the implications for the 'difference versus disability' debate; as well as consider possible wider tensions of biomarker research in relation to issues such as pre-natal screening and reproductive choice, and identity and inclusion for individuals on the autistic spectrum. Finally, we will summarize the most promising

research on blood biomarkers for autism, describing the required steps to take a putative biomarker from the 'bench to the bedside'. This educational symposium brings together researchers from scientific, ethical and psychological disciplines to provide a unique perspective on the utility of biomarkers for ascertaining autism risk, aiding in diagnosis and identifying therapeutic targets, all within the framework of the relevant ethical and social considerations.

101.001 Scientific Challenges in the Development of Putative Autism Biomarkers. L. Hewitson*, *The Johnson Center for Child Health and Development*

Background: With a strong genetic basis and many known comorbidities, autism is a very complex disorder. Current diagnostic methods and screening tools are somewhat subjective and are difficult to use in very young children. A biological marker that could predict autism risk or assist in early diagnosis would have great clinical utility. Additionally, biomarkers could provide targets for therapeutic intervention. While research in this field has greatly increased in recent years, progress has been limited and no biological markers for autism have been found to be universal.

Objectives: The objective of this presentation is to describe the major scientific challenges associated with the identification of biological markers for autism. Factors that may play a role in impeding progress in autism biomarker research, including the heterogeneity of autism, the presence of comorbid conditions, gender bias, and the availability of appropriate research samples, will be critically reviewed.

Methods: The complex heterogeneity of autism underscores the importance of recognizing different autism subtypes in relation to how biomarker studies are designed. A number of previous autism biomarker studies are clouded by methodological concerns, such as small samples sizes, lack of stringent diagnostic assessments, unsuitable controls, disparate age ranges between controls and cases, and the use of medications. The issue of gender-bias should also be carefully considered. If study designs do not take gender into account, we risk not only doing harm (such as extrapolating the utility of biomarkers based on male samples to females), but also missing critical opportunities to further our understanding of the etiology of autism. The implications of these

issues, as well as the proposed changes for DSM-5 diagnostic criteria for autism spectrum disorders, will be reviewed in terms of sub-grouping subjects for future biomarker studies. This presentation will also provide information on available research resources including various autism biorepositories and the types of datasets, tissues and samples available to researchers wishing to engage in biomarker studies.

Results: At the end of this presentation, attendees will be able to critically review the major scientific challenges associated with the identification of biological markers for autism.

Conclusions: The search for autism biomarkers in the laboratory is an important research endeavor that is fraught with many challenges, yet the translation of such findings into the clinic may be the real challenge and requires the investigation of large, well-characterized sample cohorts with appropriate controls. Only when these issues are addressed prior to implementing new studies, will robust and reliable biomarkers for autism be identified.

101.002 Social Challenges and Opportunities Surrounding the Development of Biomarkers for Autism. N. Humphrey*, *University of Manchester*

Background: A biological marker that could predict autism risk in a young child or assist in early diagnosis would have great clinical utility and could provide targets for therapeutic intervention. However, the development of such a marker may also create challenges in relation to stigmatisation, identity and social exclusion among individuals on the autistic spectrum. In Molloy and Vasil's terms, it may lead to the 'pathologising of difference' (2002).

Objectives: This presentation will consider the social issues relating to the development of biomarkers for autism. Specifically, the learning objectives are to: (1) identify and discuss the implications of autism biomarker research for the 'difference versus disability' debate; and (2) consider possible wider tensions of said research in relation to issues such as identity and inclusion for individuals on the autistic spectrum.

Methods: This presentation will explore the implications of biomarker research for a variety of

social issues pertaining to autism. The tensions between the medical and social models of disability will be used as a starting point. The focus will then shift to current debate relating to the notion of autism as a difference or disorder (Ellisman, 2011) and how biomarker research may influence this discourse. The discussion will broaden to consider concurrent implications for issues of professional terminology and semantics, the construction of identity in relation to disability among individuals with autism (Baines, 2012), access to services, challenges to diagnostic approaches to the autism spectrum (Allred, 2009), schooling and education (Humphrey & Lewis, 2008), and stigmatization and social exclusion (Kurzban & Leary, 2001).

Results: At the end of this presentation, attendees will understand the variety of social issues pertaining to the development of autism biomarkers.

Conclusions: The potential scientific and clinical advantages of autism biomarkers must be examined in relation to the many social challenges that this line of research may present. Of paramount importance here is the consideration of the views of individuals on the autistic spectrum themselves.

Allred, S. (2009). Reframing Asperger syndrome: lessons from other challenges to the DSM and ICDH approaches. *Disability and Society*, 24, 343-355.

Baines, A. D. (2012). Positioning, strategizing, and charming: How students with autism construct identities in relation to disability. *Disability and Society*, 27, 547-561.

Ellisman, L. (2011). Asperger's syndrome: Difference or disorder? *The Psychologist*, 24, 114-117.

Humphrey, N. & Lewis, S. (2008). 'Make me normal': the views and experiences of pupils on the autistic spectrum in mainstream secondary schools. *Autism*, 12, 23-46.

Kurzban R. & Leary, M. R. (2001). Evolutionary origins of stigmatization: The functions of social exclusion. *Psychological Bulletin*, 127, 187-208.

Molloy, H. & Vasil, L. (2002). The social construction of Asperger Syndrome: The pathologising of difference? *Disability and Society*, 17, 659-669.

101.003 Biomarkers for Autism: Ethical Issues Arising From Their Use in Diagnosis and Screening. P. Walsh*, *King's College London*

Background: It is hoped that the development of biomarkers for autism would not only substantially advance research into the causes of autism but could also be clinically useful in complementing or improving the current behavioural diagnosis of the condition and enabling its earlier detection, thereby assisting in the validation of very early, targeted interventions. While a number of key scientific challenges to the development of biomarkers for autism remain to be overcome, the prospect of their development means that it is both appropriate and timely to consider the ethical issues likely to arise from such scientific advances.

Objectives: This presentation will identify and analyse the ethical issues relating to the development of biomarkers for autism. More specifically, it will consider the ethical implications of using biomarkers for autism in the context of diagnosis and screening.

Methods: The presentation will explore the vexed issues associated with the heterogeneity of autism and how this affects the use of biomarkers for autism. For instance, while it is claimed that biomarkers would assist in complementing and improving diagnosis currently based exclusively on behavioural criteria, it is hard to see how biomarkers could circumvent the ethical problem of establishing a non-arbitrary cut-off point between behaviour considered 'normal' and behaviour considered 'disordered', with all the implications that has for how individuals see themselves, how others view them and how they are viewed by services, teachers, employers and so on. When it comes to using biomarkers as screening tools, the complexity and heterogeneity of autism means, it is unlikely that a single biological test or biomarker will be able to establish the risk of autism in an embryo or fetus with a high degree of certainty in the vast majority of cases. However, it is possible that

biomarker discovery may help to identify different typologies within the autism spectrum, providing parents with a probabilistic estimation of the symptoms and course of autism if the condition were to be manifested. As parental decision-making is likely to be influenced by future biomarker information about autism, the ethical implications of biomarker discovery for genetic counselling, for the choices offered to parents, and for reproductive choices more generally, will be explored.

Results: At the end of this presentation, attendees will be able to identify and understand the main ethical issues relating to the use of biomarkers for autism for diagnostic and screening purposes.

Conclusions: The current absence of systematic input from the community affected by autism is a major challenge to be overcome, given the importance of the ethical issues arising from the development of biomarkers for autism. By contextualising existing and new research knowledge within the real-life experiences of affected families, science communication regarding autism biomarkers can serve its primary purpose of informing the public and contributing to ethically informed knowledge translation.

101.004 The Status of Biomarker Research for Autism Spectrum Disorders: Recent Progress and Future Directions. P. Ashwood*, *The M.I.N.D. Institute, University of California, Davis*

Background: Autism spectrum disorders (ASD) are complex and heterogeneous with a spectrum of diverse symptoms and co-morbidities. A reliable biomarker for ASD may help provide invaluable insight to elucidate mechanisms of action that underlie the causes of autism, as well as provide possible therapeutic targets or for monitoring of treatment. Mounting evidence from a number of disciplines suggests a link between immune dysfunction and ASD. Although the causes of ASD have yet to be identified, genetic studies have uncovered many candidate genes relating to immune regulation that are altered in ASD, while peripheral markers of immune activity are often associated with greater impairments in behaviors. Epidemiological and animal studies also suggest a relationship between maternal

immune disturbances during pregnancy and changes in neurodevelopment.

Objectives: This presentation will summarize the current status of biomarker research for ASD, primarily focusing on immune parameters as targets of emerging interest for biomarker discovery. Specifically, this presentation will: (1) describe the role of the immune system in ASD with respect to the development of blood biomarkers; (2) summarize different examples of immune based biomarkers for ASD; (3) provide rationale for selected biomarkers that could guide potential treatments, and; (4) discuss emerging targets as putative biomarkers.

Methods: Decades of research have identified numerous systemic and cellular immune abnormalities in individuals with ASD and their families, providing compelling targets to explore as biomarkers. The changes in immune cell number, differences in cytokine and chemokine production, presence of brain-reactive antibodies and alterations of cellular function at rest and in response to immunological challenge in ASD will be described. While changes in immune responses may be associated with increasing impairment in behaviors that are core features of ASD, much remains to be understood about the precise mechanism by which the immune system alters neurodevelopment and to what extent it is involved in the pathogenesis of ASD. This presentation will provide a critical overview regarding putative immune biomarkers that are currently being researched for ASD.

Results: At the conclusion of this presentation, attendees will understand the role of the immune system in ASD with respect to the development of putative blood biomarkers.

Conclusions: With estimates of ASD as high as 1% of children, ASD is a major public health issue. Improvements in our understanding of the interactions between the nervous and immune system during early neurodevelopment and how this interaction is different in ASD will have important implications for the development of potential biomarkers for ASD, as well as therapeutic implications with wide ranging benefits.

Late-Breaking Abstracts Program 102 Late Breaking Abstracts

102.001 Randomized, Controlled, Phase 2 Trial of STX209 for Social Function in ASD. J. Veenstra-VanderWeele*¹, L. Sikich², R. Melmed³, J. S. von Hehn⁴, K. L. Walton-Bowen⁴, N. Kuriyama⁴, M. Cherubini⁴, P. Zarevics⁴, R. L. Carpenter⁴, M. F. Bear⁵, P. Wang⁴ and E. H. Cook⁶, (1)*Vanderbilt University*, (2)*The University of North Carolina @ Chapel Hill*, (3)*Southwest Autism Research Center and Melmed Cente*, (4)*Seaside Therapeutics*, (5)*MIT & HHMI*, (6)*University of Illinois at Chicago*

Background: STX209 (arbaclofen) is a selective GABA-B agonist associated with behavioral improvements and disease-modifying effects in animal models of fragile X syndrome (FXS). It is hypothesized to modulate mGluR5 receptor signaling, and to augment inhibitory neurotransmission.

In a previous 8-week, open-label study of 32 subjects with Autism Spectrum Disorder (ASD), STX209 was associated with significant improvement on the ABC-Lethargy/Social Withdrawal (ABC-LSW) subscale, the Social Responsiveness Scale, and the Vineland Adaptive Behavior Scales, Second Edition (VABS) Communication domain. In a placebo-controlled trial in 63 subjects with FXS, STX209 was associated with significant improvement on the ABC-Social Avoidance subscale, which is specifically validated for FXS. VABS Socialization scores also improved in the subgroup of 27 subjects with more severe social impairments.

Objectives: To examine the efficacy, safety, and tolerability of STX209 in patients with ASD, age 5-21 years.

Methods: A 12-week, double-blind, placebo-controlled trial was conducted at 24 sites in the USA. Subjects met DSM-IV criteria for Autistic Disorder, Asperger's Disorder, or PDD-NOS and had a minimum score of 8 on the ABC-LSW subscale. Up to 2 concomitant psychoactive medications were permitted, excluding antipsychotics and medications with anxiolytic effects.

Subjects were randomized to either STX209 or placebo, with stratification by age and concomitant use of psychoactive medication. Study drug was titrated over 4 weeks, to a

maximum of 10 mg TID (age 5-11 years) or 15 mg TID (age 12-21 years), with fixed dosing for the subsequent 8 weeks. Efficacy assessments included the ABC subscales, CGI-I, CGI-S, and VABS Social and Communication domain scores.

Results: 150 subjects (124 male; 130 DSM-IV Autistic Disorder; 120 ADOS-Autism) were randomized in the study, with 26 receiving at least one concomitant psychoactive medication. 130 subjects completed the study, with 10 (8 on STX209, 2 on placebo) discontinuing due to adverse events, which were generally behavioral (e.g., aggression, sleep disturbances). There were 2 serious adverse events (suicidal ideation on STX209; anaphylaxis on placebo). Suicidal ideation also occurred in 1 subject on placebo. Overall, STX209 was well-tolerated, with a 9% incidence of somnolence.

On the primary endpoint, the ABC-LSW subscale, subjects on STX209 and placebo showed very similar improvements (change from baseline -5.4±0.78 vs. -6.0±0.75, LS mean±SEM, p=0.518). On the CGI-S, subjects improved significantly more on STX209 (-0.6±0.10 vs. -0.2±0.10, p=0.006). On all other secondary endpoints, results favored STX209 numerically, but did not reach statistical significance (e.g., VABS Socialization standard score: 3.8±1.27 vs. 2.1±1.22, p=0.362). In a post-hoc analysis among subjects whose Vinelands were completed by the same clinician and caregiver (n=96), as the study protocol had required, those receiving STX209 showed greater improvement on the VABS Socialization scale (7.2±1.40 vs. 1.8±1.27, p=0.006). Subgroup analyses indicated that improvement on VABS Socialization scores was notably larger in subjects with IQ≥70.

Conclusions: STX209 was well-tolerated and shows potential for clinically-meaningful improvements in social function. Drug effects were more evident in subjects with higher IQs. Further prospective trials of STX209 are needed.

102.002 Adaptive Intervention For Communication In Minimally Verbal School Aged Children. C. Kasari¹, A. P. Kaiser^{*2}, K. Goods³, M. Y. Roberts², P. Mathy⁴, R. Landa⁴, C. Mucchetti⁵ and D. Almirall⁶, (1)University of California, Los Angeles, (2)Vanderbilt University,

(3)University of California Los Angeles, (4)Kennedy Krieger Institute, (5)UCLA, (6)University of Michigan

Background: Current estimates are that 30-40% of children with autism spectrum disorder (ASD) are minimally verbal at age 5 years despite involvement in intensive early interventions. Current successful behavioral interventions, such as joint-attention and engagement with enhanced milieu training (JAE/EMT), improve social communication and spontaneous use of spoken words in children who are preverbal (preschool aged). However, these interventions have not been rigorously tested for minimally verbal school-aged children with ASD, despite the high prevalence and severity of need of this population. The IACC, NIH, and Autism Speaks all have placed a high priority on developing efficacious interventions for these children. Further, there is significant interest in the effectiveness of blending behavioral interventions with augmentative alternative communication (AAC) devices to speed the uptake of spoken communication.

Objectives: An adaptive intervention is a sequence of decision rules, which adjusts treatment over time as a function of the changing clinical status of the child. The overarching aim of this study was to construct and systematically test an *adaptive intervention* that utilizes JAE/EMT and varies the addition of an AAC device with minimally verbal school aged children. The primary specific aim of this study was to examine the effect of an adaptive intervention beginning with JAE/EMT+AAC versus with JAE/EMT alone.

Methods: Sixty children participated in a longitudinal randomized clinical trial across 3 sites (UCLA, Vanderbilt, and KKI). At baseline, participants completed diagnostic (ADOS), and cognitive (Leiter-R) assessments. To measure spontaneous communication, participants completed a natural language sample (NLS) with a blind assessor at entry, intervention mid-point (month 3), and exit (month 6). Children were randomly assigned to JAE/EMT+AAC or JASP/EMT without AAC. Intervention sessions were two, hour-long sessions per week. Intervention was adapted at mid-point based on whether the child was an early or slow responder. Early or slow response status was based on spontaneous communication during intervention sessions and the NLS. Intervention was intensified (to three sessions per week) for JAE/EMT+AAC participants

who demonstrated slow-response. JAE/EMT participants who demonstrated slow-response were had treatment intensified or had were introduced an AAC.

Results: Fifty-nine of the children met criteria for autism, and 1 met for ASD (ADOS). Participants were an average of 6.33 years old ($SD=1.12$), had an average of 16.62 ($SD=14.63$) unique words on the baseline NLS, and average nonverbal cognitive scores of 4.01 years ($SD=1.13$, Leiter-R). At mid-point, adaptive interventions beginning with JAE/EMT+AAC had a larger total number (Cohen's $d=0.76$, $p<0.01$) and percent ($d=0.59$, $p=0.02$) of spontaneous communicative utterances versus adaptive interventions beginning with JAE/EMT alone. The effects persist through treatment exit: total number ($d=0.6$, $p=0.02$) and percent ($d=0.75$, $p<0.01$) of spontaneous communicative utterances.

Conclusions: These data suggest that children who are minimally verbal can make significant progress in socially communicative spoken words after age 5. Moreover, they benefit significantly more from the experimental intervention when they begin the treatment with an AAC device than without. Thus, future research should examine how AAC support can be integrated into homes and schools to further improve communicative outcomes for these children.

102.003 The Autism Epidemic Hypothesis: the Association of Autism With Age in the General Population. T. Brugha* and F. Tyrer, *University of Leicester*

Background:

Increasing diagnoses of autism, most notably in multi centre research in the USA, (Centers for Disease Control and Prevention, 2012) has underpinned belief in an autism epidemic. If the increase is valid – meaning a true increase in cases and not just in case recognition – the implications are profound and urgent for identifying causes likely to be novel and potentially controllable (www.nimh.nih.gov/about/director/index.shtml). The most important recent evidence against the autism epidemic hypothesis is a 2011 British adult general population survey showing no significant difference in prevalence by age (Brugha et al, 2011). However to date this finding from a

community survey of over 7000 adults able to take part in a health survey has not been replicated. As part of an extension of the 2011 survey (Brugha et al, 2012) adults with intellectual disability were studied and the association of autism with age was examined.

Objectives:

As part of a prevalence survey of autism in an epidemiological study of adults with intellectual disability unable to take part in a general population health survey, to examine further the association of autism with age.

Methods:

Sampling was based on population case registers of adults with intellectual disability in three parts of England. Adults were living in institutions (communal care establishments) or in private households (excluding anyone able to participate in a health survey interview). Phenotyping was primarily based on the age appropriate module of the ADOS (modules 1 and 4) in phase one of a two phase survey design in which a stratified subsample were also assessed with the ADI-R and DISCO.

Results:

A total of 290 interviews were conducted with intellectually disabled adults. 89 autism cases were identified. Analyses are being undertaken examining the association of autism with age and other factors and possible confounders, with work on the interpretation of findings still ongoing.

Conclusions:

Challenges to the interpretation of findings include reduced survival in this population, constraints on autism assessment in the most profoundly intellectually impaired adults and issues of statistical power. Further work in the general population is also planned.

References

1. Brugha, T., Cooper, S. A., McManus, S., et al (2012) Estimating the Prevalence of Autism

Spectrum Conditions in Adults: Extending the 2007 Adult Psychiatric Morbidity Survey. (ed C. a. M. H. T. The NHS Information Centre), pp. 31. Leeds: The NHS Information Centre.

2. Brugha, T. S., McManus, S., Bankart, J., et al (2011) Epidemiology of autism spectrum disorders in adults in the community in England. *Archives of General Psychiatry*, 68, 459-466.

3. Centers for Disease Control and Prevention (2012) Prevalence of Autism Spectrum Disorders — Autism and Developmental Disabilities Monitoring Network, 14 Sites, United States, 2008. (ed Centers for Disease Control and Prevention), pp. 19. Atlanta: Centers for Disease Control and Prevention.

102.004 A Suppressor Screen of Mouse *Mecp2* Implicates Cholesterol Metabolism in Rett Syndrome. C. M. Buchovecky^{*1}, S. M. Kyle¹, S. D. Turley² and M. J. Justice¹, (1)*Baylor College of Medicine*, (2)*University of Texas Southwestern Medical School*

Background:

Rett Syndrome is a severe X-linked disorder with a prevalence of approximately one per 10,000 live female births. It presents with developmental regression, including loss of speech, motor impairments and autistic features. Loss-of-function mutations in methyl CpG binding protein 2 (MECP2) cause more than ninety-five percent of cases. *Mecp2*-null mouse models recapitulate many aspects of the human disease. Symptoms can be reversed by restoration of *Mecp2* function in symptomatic mice, and partially rescued with other factors. This provides substantial evidence that therapeutic intervention in Rett Syndrome is possible. Unfortunately, as a widespread epigenetic factor, MECP2 levels are extremely dosage sensitive, making direct manipulation a poor treatment option.

Objectives:

MECP2 has multiple binding partners and its mutation impacts many biological pathways in Rett Syndrome, but it is unclear which are relevant to symptom progression. Our use of forward genetics allowed us to dispense with *a priori* beliefs about MECP2 function. In this way, we are able to identify novel binding partners and downstream pathways that, when altered, effect the amelioration of symptoms. Any such pathway

could contain potential targets for the development of new pharmacological treatments for Rett Syndrome.

Methods:

Studies were carried out in the *Mecp2^{tm1.1Bird}* deletion mouse model. We employed a dominant ENU mutagenesis screen to identify biological pathways important for symptom suppression. We capitalized on genetic variation between the C57BL/6J and 129S6/SvEv mouse strains to locate five suppressing mutations through a combination of SNP linkage mapping and whole exome sequencing strategies. One is a loss-of-function mutation in squalene epoxidase (*Sqle*), a rate-limiting enzyme in committed cholesterol biosynthesis. Cholesterol and lipid concentrations were assessed by gas-liquid chromatography, synthesis was assessed from saponified tissue after tritium incorporation, and sterol intermediates were measured by tandem mass spectrometry.

Results:

The loss-of-function *Sqle* mutation increased longevity and improved motor functioning, activity levels and overall health in *Mecp2*-null mice. Based on the biochemical role of SQLE, we examined cholesterol and lipid metabolism in the *Mecp2*-null male mice and found perturbations in both the brain and liver. Similar, but delayed perturbations were found in *Mecp2* heterozygous females. Accordingly, we treated *Mecp2* mutant mice with cholesterol-lowering statin drugs and found that they also alleviate motor symptoms and confer increased longevity in both males and females.

Conclusions:

The discovery of a Rett Syndrome suppressing mutation in the cholesterol biosynthesis pathway was unexpected and unlikely to have been found using the reverse genetics approach that is more common in mouse research. Cholesterol metabolism represents a potential pathway for new therapeutic targets to treat the syndrome. Our data add to a growing body of evidence that cholesterol plays an important role in many neurological diseases. More broadly, the results of

this study suggest researchers working on autism-related disorders would benefit from the use of a systems biology approach to identify targetable downstream pathways involved in their pathogenesis.

102.005 Prenatal Exposure to Autism-Specific Maternal Autoantibodies Impairs Proliferation of Neural Precursor Cells, Neuronal Morphology and Animal Behavior. V. Martinez Cerdeno*, *Institute for Pediatric Regenerative Medicine*

Background:

Autism spectrum disorders (ASD) are a group of etiologically and phenotypically heterogeneous neurodevelopmental disorders manifesting in early childhood, currently estimated to affect 1 in 88 children. ASD is defined by core deficits in communication and reciprocal social interaction, and by the presence of repetitive or stereotypical behavior. Autoantibodies to fetal brain proteins, described previously by our laboratory, are found exclusively in a sub-population of mothers whose children are diagnosed with autism spectrum disorder.

Objectives:

We show that maternal auto-antibodies interfere with prenatal development of the embryonic cerebral cortex. In previous passive transfer models, the presence of human IgG antibodies directed against fetal brain proteins during gestation has been shown to produce autism-like behavior in the offspring. The next logical step in elucidating the mechanism by which the maternal autoantibodies affect the developing brain was to examine local effects during the embryonic period. We investigated the impact of these autism-specific maternal antibodies on the neurogenic stem cells in the developing brain. We also investigated the impact of maternal autoantibody exposure on the histology, cellular composition, and neuroanatomy of the mature cerebral cortex.

Methods:

We passively transferred purified human IgGs directly into the cerebral ventricles of mouse embryos during mid-neurogenesis and examined stem cell proliferation at later stages of development.

Results:

We found that maternal autoantibodies increased proliferation in the subventricular zone of the embryonic cerebral cortex. We show that the brains of animal prenatally exposed to autism-specific maternal autoantibodies were bigger, weighed more, and that cortical neuron size was significantly increased. Finally, we investigated the effect of *in utero* exposure to brain-reactive maternal IgG antibodies on social and stereotypical behavior of the offspring. We show that the anatomical changes in the adult cerebral cortex that were produced by maternal autoantibody exposure are concomitant with changes in the behavior that are associated with the core features of autism.

Conclusions:

In conclusion, we show that exposure to maternal autoantibodies alters the neural precursor cell profile in the embryonic proliferative zones, the morphology of adult neurons in the cortex, and the behavior of adult mice exposed to maternal autoantibodies during prenatal development. We propose that prenatal exposure to maternal autoantibodies may constitute a viable mechanism for one type of previously unrecognized prenatal risk factor for autism spectrum disorders.

102.006 Resolution of the Factoral Structure of Quantitative Autistic Symptomatology in 11, 000 Assessments of School-Aged Children and Adults. T. W. Frazier¹, C. Gruber², P. A. Law³ and J. N. Constantino*⁴,
(1)*Cleveland Clinic Lerner College of Medicine*,
(2)*Western Psychological Services*, (3)*Kennedy Krieger Institute*, (4)*Washington University School of Medicine*

Background: Understanding the factor structure of autism is critical to the discovery and interpretation of causal mechanisms in autistic syndromes. Newly-identified susceptibility factors involving single gene mutations, co-occurring variations in small groupings of risk genes, or the effects of a multitude of common variations—occurring in specific combinations and jointly influencing risk—are being elucidated every month. In order to examine specific associations between behavioral variations and their underlying genetic and neural causes, it is important to continue to explore and resolve questions about how traits and symptoms in

autistic syndromes co-vary, using data from large, diverse populations that encompass the full range of symptom structures underlying autism spectrum disorders (ASD).

Objectives: To evaluate the factor structure of quantitative autistic traits in a large, diverse sample of children and adults, representing the full range from typical (general population) variation to severe, clinical-level affectation. Confirmatory factor analysis and assessment of measurement invariance across age, sex, informant, and ASD diagnosis (within autism-affected families) were examined in the largest sample ever assembled for this purpose.

Methods: Data were acquired using the Social Responsiveness Scale-2 (SRS-2) from three distinct samples: 1) a child clinical sample involving children affected by ASD and their unaffected siblings, participating in the Interactive Autism Network (IAN) volunteer registry (N=7,921) and reported-upon by their parents; 2) a child population-based sample (N=1,012) rated by a parent; and 3) an adult population-based sample (N=702) in which at least one report was obtained from a relative or other close acquaintance (n=1573), and in addition most subjects provided a self-report (n=673). Confirmatory factor analysis and assessment of measurement invariance were implemented on the accumulated data set.

Results: A two-factor structure differentiating social-communicative impairment (SCI) and restricted repetitive behaviors (RRB)--as elaborated in the updated DSM-5 criteria for autism spectrum disorders--exhibited a highly acceptable model fit when confirmatory factor analysis was applied to the data. These factors exhibited measurement invariance across age, sex, and reporter (self vs. other), but exhibited a somewhat lower level of measurement equivalence between clinical and non-clinical populations. The statistical power afforded by this large sample allowed further factorial separation within each of the two principal factors, yielding three SCI sub factors (emotion recognition, social avoidance, and interpersonal relatedness) and two RRB sub factors (insistence on sameness and repetitive mannerisms). Cross-trait correlations between SCI and RRB remained extremely high, i.e. on the order of 0.95 for the general

population, 0.94 for unaffected siblings in ASD-affected families, and 0.87 among children affected by ASD.

Conclusions: This study provided strong evidence of separable, but highly correlated, autism traits corresponding to DSM-5 domains. The statistical power afforded by quantitative analysis in this large sample allowed resolution of sub factors (themselves highly inter-correlated) which potentially represent subtle aspects of differentiation between deficits in emotion recognition, social avoidance, and interpersonal relatedness in autism and related neuropsychiatric syndromes. These components of behavioral dysfunction may constitute important targets for intervention, and for association with biological markers, particularly in gene discovery and in the exploration of neural signatures of autism.

102.007 Modeling the Phenotypic Architecture of Autism Symptoms From Time of Diagnosis to Age 6. S. Georgiades^{*1}, M. Boyle¹, P. Szatmari¹, S. Hanna¹, E. Duku¹, L. Zwaigenbaum², S. E. Bryson³, E. Fombonne⁴, P. Mirenda⁵, I. M. Smith³, W. Roberts⁶, T. Vaillancourt⁷, J. Volden², C. Waddell⁸, T. Bennett¹, M. Elsabbagh⁹ and A. Thompson¹, (1)*Offord Centre for Child Studies & McMaster University*, (2)*University of Alberta*, (3)*Dalhousie/TWK Health Centre*, (4)*Montreal Children's Hospital*, (5)*University of British Columbia*, (6)*University of Toronto*, (7)*University of Ottawa*, (8)*Simon Fraser University*, (9)*McGill University*

Background: Autism Spectrum Disorder (ASD) is a heterogeneous disorder. Recent studies showed that ASD heterogeneity can be captured by classifying newly diagnosed children into three classes (or subgroups) that differ in symptom severity and configuration (Georgiades et al., 2013). Despite the fact that notable progress has been achieved in the classification of children with ASD at the time of diagnosis, longitudinal research is needed to better understand how symptom heterogeneity unfolds as children with ASD develop.

Objectives: The main objective of the current study was to model the underlying latent class structure (phenotypic architecture) of core autism symptoms - social communication deficits (SCD) and Fixated Interests and Repetitive Behaviours (FIRB) - from the time of diagnosis to age 6.

Matthews¹, X. Z. Zhang², B. Auyeung¹, S. Baron-Cohen¹ and C. Brayne¹, (1)*University of Cambridge*, (2)*Peking University First Hospital*

Background:

There are few epidemiological studies and limited knowledge of ASC in mainland China. Modern screening and standardised diagnostic instruments have not been adopted in mainland China, which makes comparison of the prevalence of Autism Spectrum Conditions (ASC) in the East and West difficult.

Objectives:

1. To test the utility of a screening instrument for ASC, a Mandarin Chinese version of the Childhood Autism Spectrum Test (CAST);
2. To apply standardised diagnostic instruments to a Chinese population for diagnosis confirmation for the first time;
3. To establish a prevalence estimate of ASC in an undiagnosed population in mainland China;
4. To validate the existing diagnosis of ASC in mainland China.

Methods:

We followed the design used previously in the UK (British J. Psychiatry, 2009). The Mandarin CAST was validated through screening two primary school pupils (N = 737 children age 6-10 years old) in Beijing and by conducting diagnostic assessments with a proportion of the screened children using the ADOS and ADI-R. The prevalence estimate was generated using the inverse probability weighting. The number of undiagnosed children in mainstream schools was calculated after adjusting and imputing for missing values (including age, sex and non response effects). The test-retest reliability of the Mandarin CAST was examined in the assessment sample of the validation (N=103) using Cohen's Kappa, and the exploration of the psychometric properties was conducted in the validation sample using categorical data factor analysis (CDFA) and the item response theory (IRT). N = 50 cases with an existing diagnosis of autism were also re-examined using the ADOS and ADI-R.

Results:

Methods: The sample comprised 280 children (86% males) participating in a longitudinal study of ASD. Factor mixture modeling (FMM) was performed using data on 26 items from the Autism Diagnostic Interview – Revised algorithm indexing the SCD and FIRB autism symptom domains. A set of goodness-of-fit criteria were used to select the best fitting model of the underlying latent class structure of autism symptoms. The FMM analysis was repeated twice – at time of diagnosis (Time 1) and when the children turned age 6 (Time 2).

Results: At Time 1, a “2-factor/3-class” structural model provided the best fit to the data (Class 1=35%; Class 2=11%; Class 3=54% of the sample). This model replicates the one reported in the Georgiades et al. (2013) study. However, the same model failed to converge at Time 2 at which point a more parsimonious “2-factor/2-class” model provided the best fit to the data (Class A=32%, Class B=68% of the sample). According to this factor mixture model 6-year old children with ASD can be classified in two distinct classes characterized by significantly different levels of severity on the SCD and FIRB symptom dimensions. Compared to children from Class B, children in Class A have significantly higher adaptive and language skills and present with lower emotional/behavioural problems. Furthermore, there is a difference in the way boys and girls are distributed across the two ASD classes; girls tend to be assigned to the less severe, higher functioning class (Class A: 61.5%; Class B: 38.5%) while the reverse is true for boys (Class A: 27.4%; Class B: 72.6%). Finally, children across the two classes did not differ in terms of the age at which they were diagnosed.

Conclusions: Study findings suggest that there is a change in the underlying latent class structure of autism symptoms during the first few years after diagnosis. Specifically, it appears that there is a reduction in symptom heterogeneity in children with ASD from the time of diagnosis to age 6. These findings demonstrate the dynamic nature of the ASD phenotype and speak to the importance of repeated classification assessments of symptoms, functional skills, and behaviours as children develop.

Response was high (97%). Using the UK cut-off (≥ 15), CAST performance was 84% sensitivity and 96% specificity (95% CI 46, 98 and 96, 97 respectively). 6/103 children, not previously diagnosed, were found to meet diagnostic criteria (8.5 after adjustment, 95% CI: 1.6, 15.4). The preliminary prevalence in an undiagnosed primary school population in mainland China was 119 per 10,000 (95% CI: 53, 265). Of 50 children with an existing diagnosis of autism by Chinese clinicians, 47 children met the diagnosis of autism on the ADOS and 44 children met the diagnosis of autism on the ADI-R. Using a cut-off score of 15, the test-retest reliability was good ($Kappa=0.64$). The test-retest reliability in three categories (≤ 11 , 12-14, ≥ 15) was moderate (Weighted $Kappa=0.53$). The exploratory factor analysis proposed a two-factor solution for the Mandarin CAST which comprised Social and Communication, and Inflexible/Stereotyped Language and Behaviours.

Conclusions:

The utility of CAST is acceptable as a screening instrument for ASC in large epidemiological studies in China. There are undiagnosed children on the autism spectrum in primary schools in the general population in China. Using a comparable method, the preliminary prevalence estimate of ASC in mainland China is similar to that of Western estimates. Because this was only based on 2 schools ($n = 737$ children), a larger-scale prevalence study is now underway to confirm this preliminary estimate, in 14 regions across China with the aim of screening $n = 20,000$ children per region.

Clinical Phenotype Program

103 Clinical Phenotype

103.001 Sensory Subtypes in Children with ASD and Associated Outcomes: Latent Profile Transition Analysis Using a National Survey of Sensory Features. K. K. Ausderau¹, G. T. Baranek², J. Sideris³, M. Furlong², L. M. Little² and J. Bulluck², (1)University of North Carolina, (2)University of North Carolina at Chapel Hill, (3)Frank Porter Graham Child Development Institute

Background: Sensory features are prevalent in children with ASD and will soon be associated with the core characteristics. The heterogeneity of sensory features has long been discussed but

lacking in the literature is the identification of homogeneous sensory phenotypes as well as assessing the stability of such identified subtypes overtime.

Objectives: This study uses latent profile transition analysis (LPTA) to identify sensory subtypes, assess their stability overtime, and presents association of the subtypes to child characteristics and functional outcomes (i.e., Vineland Adaptive Behavior Scale-II (VABS) and Parenting Stress Index Short Form (PSI)).

Methods: Data were collected from participants with ASD, ages 2-12, at two time points (Time 1, $n = 1307$, Time 2, $n = 884$), one year apart as part of a national online survey. A confirmatory factor analysis (CFA), of the Sensory Experience Questionnaire-3.0 (SEQ-3.0) yielded four factors of sensory response patterns (i.e., hyporesponsiveness; HYPO, hyperresponsiveness; HYPER, sensory interests, repetitions, and seeking behavior; SIRS, and enhanced perception; EP). These scores were exported for an LPTA. Previous literature, latent profile analysis (LPA) from both time points, LPTA with multiple profile solutions, and assessing statistical fit (AIC, BIC, Lo-Mendell-Rubin test, entropy, and the Bootstrap Likelihood Ratio Test) were used to determine the appropriate number of distinct subtypes overtime. The final LPTA was run with select child and family covariates as well as outcome measures.

Results: Four distinct sensory subtypes were supported by statistical measures and theoretical/clinical models. Participants ($n = 971$, 91%) remained stable in their sensory subtype across one year. The first subtype ($n = 297$, 31%) described children who scored low on all sensory patterns, while the second subtype ($n = 189$, 19%) showed the opposite profile, with high scores in all four sensory patterns. The third subtype ($n = 294$, 30%) scored very close to the mean on all patterns, with a tendency to score low on HYPO and SIRS, but higher on HYPER and EP. The fourth subtype ($n = 191$, 20%) had the opposite pattern of the third subtype with scores more extreme on HYPO and SIRS. The four sensory subtypes related differentially to outcome measures. The first subtype (81.38) had the highest VABS Adapted Behavior Composite score, followed by the third (79.84), second (70.65), and fourth (61.56) subtypes. The first and third subtypes

were not significantly different. However, the second and fourth subtypes were significantly different from each other as well as the other two subtypes. The first (89.05) subtype had the lowest PSI total score followed by the third (96.64), fourth (103.15), and second (108.97) subtype. The second and fourth subtypes were not significantly different from each other. However, the first and third subtypes were significantly different from each other as well as the other two subtypes.

Conclusions: The LPTA identified four distinct sensory subtypes that were stable over one year in a population of children ages 2-12 with ASD. The identification of homogenous sensory subtypes and characterization of children within their subtype to functional outcomes and demographic variables will lead to improved assessment, treatment and potentially inform biological mechanisms.

103.002 Sensory Hyposensitivity Is Associated with More Severe Clinical Presentation in Autism Spectrum Disorders. D. A. Zachor*¹ and E. Ben Itzhak², (1)*Tel Aviv University / Assaf Harofeh Medical Center*, (2)*Ariel University Center/ Assaf Harofeh Medical Center*

Background:

Sensory processing difficulties have been commonly described in autism spectrum disorder (ASD) and have been considered a prominent feature in the clinical presentation. A sensory processing dysfunction subscale has been added recently to the restrictive and repetitive behaviors (RRB) domain criteria for ASD in the new DSM 5.

Objectives:

The current research aims at elucidating the characteristics and impact on functioning of two common major sensory processing modalities, hypo- and hyper-sensitivities in ASD. Firstly, the frequencies of sensory hypo- and hyper-sensitivities were assessed in the entire study group. Secondly, the association between having sensory hypo- and/or hypersensitivity and the severity of the clinical phenotype in autism symptoms, cognitive ability and adaptive skills were evaluated.

Methods:

The study was conducted at 'The Autism Center' a national tertiary center involved in diagnosis, treatment and research in ASD. The cohort included 679 participants (590 males, 89 females) diagnosed with ASD, within the age range of 18 m.-15 y. (M=44.1m.±28.7). Participants underwent a neurological assessment and behavioral and cognitive evaluations by a skilled interdisciplinary team. Assessment of ASD was obtained using standardized tests, the Autism Diagnosis Interview-Revised (ADI-R), and the Autism Diagnosis Observation Schedule (ADOS). Autism severity was assessed using the ADI-R algorithm, the ADOS algorithm, and the ADOS severity scale scores. Cognitive and developmental abilities (IQ/DQ) were assessed using standardized tests and adaptive skills using the Vinland adaptive behavior scales (VABS). Information regarding sensory processing dysfunction specifically in hypo- and hyper-sensitivities, were obtained from the relevant ADI-R items with scores of one or above. Sensory hyposensitivity referred to both having seeking behaviors and tolerance to pain. Sensory hypersensitivity referred to active avoidance of one or more sensory modalities.

Results:

Sensory hyposensitivity was observed in 70.4% and sensory-hypersensitivity in 66.0% of the ASD group. The ASD subgroup with sensory hyposensitivity had significantly more severe autism symptoms than the subgroup without sensory hyposensitivity. The sensory hyposensitivity subgroup had significantly higher ADI-R scores in all the three examined domains (social interaction, communication and RRB) ($p < .001$), significantly higher scores in the ADOS algorithm, and in the autism severity scale scores ($p < .001$) than the subgroup without hyposensitivity. Regarding cognitive ability, the sensory hyposensitivity subgroup had significantly lower IQ/DQ scores than the subgroup without hyposensitivity. Regarding adaptive skills, the subgroup with sensory hyposensitivity had significantly lower VABS scores than the subgroup without hyposensitivity in: communication, daily living skills and socialization domains ($p < .001$). In contrast, the subgroup with sensory hypersensitivity had only significantly higher ADI-

R scores than the subgroup without sensory hypersensitivity and only in the RRB domain ($p < .001$). No significant differences in ADOS algorithm, autism severity scale, IQ/DQ and VABS scores were noted between the groups with and without sensory hypersensitivity.

Conclusions:

In ASD, having sensory hyposensitivity is highly associated with more severe clinical presentation affecting numerous developmental domains. It is suggested this clinical phenotype has a unique neurobiological origin. The current findings emphasize the importance of including sensory processing dysfunction as a core criterion for ASD and the need for developing specific treatment strategies to address sensory hyposensitivity.

103.003 Behavioral Topographies That Adversely Impact Dynamic Visual Scanning in Adolescents with ASD. E. M. Kim*, W. Jones and A. Klin, *Marcus Autism Center, Children's Healthcare of Atlanta & Emory University School of Medicine*

Background: Dynamic social interactions encompass rapid progressions of widely varying auditory, haptic, and visual events (e.g. gestures, gaze, verbal exchanges), all happening within complex and cluttered environments. Observers must effectively orient attention to socially relevant information while ignoring potential environmental distractors. Previous research measured dynamic visual scanning during viewing of naturalistic social situations, revealing moments when typically developing (TD) individuals allocated their visual resources in a spatially and temporally locked manner. Individuals with autism spectrum disorders (ASD) revealed significantly different visual scanning behavior. Specifically, convergence of visual resources on socially relevant events was markedly diminished, demonstrating that behaviorally salient events for TD individuals did not receive the same visual scrutiny by those with ASD. The current study will examine the specific factors that guide, fail to guide, or disrupt the deployment of preferential attention in adolescents and young adults with ASD.

Objectives: To examine dynamic visual scanning in relation to an ethological inventory of natural behaviors during video scenes of social

interaction, and to then identify specific events (e.g. facial expressions, vocalizations, movements) that either elicit or fail to elicit convergent visual scanning in individuals with ASD relative to nonautistic benchmarks.

Methods: Eye-tracking data were collected from adolescents and young adults with ASD (mean age = 16.67 (3.92) years; $n = 21$) and TD controls matched on age and verbal function (mean age = 16.86 (4.5); $n = 17$) while viewing video scenes of realistic social interactions. We used kernel density estimation to quantify the level of convergence of visual scanning at each moment in time for both groups in order to obtain measures of relative salience. Ethograms were constructed for each video, for which the onset and offset of specific events were characterized on a frame-by-frame basis, and used to examine moments when significant group-differences occurred.

Results: Preliminary analyses suggest that between-group differences in visual scanning were greatest when more actors were onscreen without camera movement, during which visual scanning by individuals with ASD exhibited considerably diminished convergence on faces that were salient to TD individuals. However, when individuals with ASD demonstrated higher convergence on faces, we found that (1) the face/s occupied greater total screen area, or (2) the actor/s made higher amplitude vocalizations and/or particular body motions. Consistent with past research, the ASD group looked more at the mouth and body regions than the eyes when looking at faces.

Conclusions: During viewing of naturalistic social situations, groups of TD and ASD individuals demonstrate significantly different patterns of dynamic visual scanning. The nature of these group differences seems largely mediated by both physical and contextual factors, with individuals with ASD at their greatest disadvantage at times when more actors were present on screen and when the visual environment was more cluttered. This appears to increase the attentional demands required by viewers, both to rapidly reallocate attention to relevant events as they unfold in time and to ignore behaviorally irrelevant distractors.

103.004 Characterization of Autism Phenotypes Using Sensory Features. A. E. Lane*¹, S. L. Bishop², C. A. Molloy³ and P. Manning-Courtney⁴, (1)*The Ohio State University*, (2)*Weill Cornell Medical College*, (3)*Harrison Community Network*, (4)*Cincinnati Children's Hospital Medical Center*

Background:

Previous studies have reported that the majority of children with autism spectrum disorders (ASD) present with behaviors and emotional responses suggestive of sensory modulation dysfunction (Tomchek & Dunn, 2007). Further, distinct profiles of sensory modulation function have been identified within ASD (Ausdureau et al 2012; Lane et al 2010, 2011; Ben-Sasson et al, 2008).

Recently, associations have been made between patterns of sensory dysfunction and the core deficits of autism, specifically, repetitive behaviors, ritualism and communication competence (Boyd et al 2010; Lane et al, 2010). Moreover, sensory symptoms have been included in the proposed DSM-V criteria for ASD diagnosis (APA, 2012). A major challenge to efforts to identify effective interventions for individuals with ASD is the heterogeneity of the disorder. Phenotyping is the classification of a disorder based on relevant physical and behavioral characteristics for the purposes of reducing heterogeneity and improving management. A systematic investigation of sensory-based phenotypes in ASD is indicated given the frequency of reported difficulties in this area and evidence of strong associations between sensory dysfunction and specific ASD symptom and behavioral profiles.

Objectives:

This study sought to: 1) confirm the existence of distinct sensory subtypes in a large sample of children diagnosed with ASD and 2) examine the relationship between sensory subtypes and age, IQ, gender, autism severity and diagnosis on the spectrum.

Methods:

We used a secondary analysis approach of data collected during diagnostic evaluations at a large, Midwestern, hospital-based center for autism services and research. Participants were 228

children diagnosed with an ASD aged between 2-10 years. Sensory symptoms were assessed via parent report using the Short Sensory Profile. Autism severity was calculated via the ADOS Calibrated Severity Score and IQ was measured using either the Mullen Scales for Early Learning or the Stanford-Binet-5. Model-based cluster analysis was used to determine the existence of distinct sensory subtypes. One-way ANOVA with post-hoc tests were used to determine differences between the subtypes on key demographic variables.

Results:

Four distinct sensory subtypes were revealed in our study supporting the results of previous reports. The subtypes differed from each other on the basis of severity of symptoms and number and type of sensory modalities affected. The four subtypes are: 1) no sensory impairment (n=84), 2) taste/smell sensitive (n=92), 3) postural inattentive (n=23) and 4) generalized sensory dysfunction (n=29). No significant differences were noted between the groups on the bases of autism severity, diagnosis on the spectrum or gender. The Taste/Smell Sensitive subtype was significantly younger than the other groups at diagnosis and had lower IQ. Age and IQ did not discriminate between the other three subtypes, however.

Conclusions:

Our study provides evidence for the utility of sensory features as a means of characterizing meaningful subgroups of children with ASD. Sensory features were able to explain variability in our sample beyond traditional measures of age, autism severity and IQ. Future studies should 1) validate these behavioral subgroupings with biomarkers and 2) investigate the utility of the subtypes in predicting intervention response.

103.005 How an Enhanced Program On Attention to Emotion Affect Viewing Preferences to Social Information in Children with Autism Spectrum Disorder (ASD): An Eye-Tracking Study. R. Siracusano*¹, L. Billeci², G. Crifaci³, M. Boncoddò¹, M. Ciuffo⁴, E. Germanò⁴, G. Tortorella¹, G. Pioggia⁵, R. A. Fabio⁴ and A. Gagliano⁴, (1)*Universita' di Messina*, (2)*CNR*, (3)*National Research Council of Italy (CNR)*, (4)*Institute of Clinical*

Physiology (IFC), (4)Università di Messina, (5)Institute of Clinical Physiology, National Research Council (CNR)

Background: Using pictures showing people (and specifically faces) within social scenes, research has concluded that individuals with autism exhibit a lack of interest in socially relevant information. They fail to orient towards socially relevant cues such as faces in a way that dissociates them from individuals without autism (Sasson et al., 2007; Klin et al; 2002b). Studies suggest that eye-tracking techniques have the potential to offer insight into the downstream difficulties in everyday social interaction which such individuals experience (Boraston Z., et al, 2007).

Objectives: In this study eye-tracking technology was applied to assess the gaze scan paths in children with autism spectrum disorders (ASD) and in typically developing peers (No-ASD) on emotional faces. We examined whether the gaze direction in children with ASD is modified by a training to help children to enhance their understanding of the causes of emotions and of emotional expressions.

Methods: A sample of 21 ASD children and 17 typical development children was recruited. A visual task, consisting of 6 social scene images (from the 1990 film of Chris Columbus "Home alone"), was shown to each participant and gaze behaviour was measured by means of eye-tracking. Different region of interest (ROIs) were defined: principal actor's face, nose, mouth and eyes, other actors' faces and objects. For each ROI the fixation count, the duration of the first fixation and the fixation time were measured. The ASD patients were divided in 2 groups: a group was submitted to an emotion recognition program (ASD-a) and the other group did not perform any training (ASD-b). After 5 weeks of training or of no-training, the same visual task and eye-tracking protocol was repeated on all ASD subjects.

Results: ASD and No-ASD differed for gaze durations to principal actor's faces. Individuals with autism spent less time than is typical viewing the faces and the eye, and more time the mouth and nose regions. The patients who completed the training, showed a tendency to scan the principal actor's face more than the ASD that did not carry out any training. Particularly, the face fixation time ($p=0.05$), the first fixation duration ($p=0.03$)

and the fixation time of nose ($p=0.03$) were significantly higher in ASD-a group than ASD-b, while the fixation count of the mouth was significantly lower in ASD-a group than in ASD-b ($p=0.03$).

Conclusions: This research, corroborating previous studies, suggests that patient with autism show atypical scan paths on emotional faces. An enhanced program on attention to emotion seems to change the viewing preferences when socially relevant information are presented to the children. An increased attention to social indicators appears to go through a qualitative and quantitative change of the look and vice versa. A better understanding of this relationship could provide useful data to increase the understanding of the mechanisms that underlie these disorders.

103.006 Parenting Behaviour in Mothers of Children with Autism Spectrum Disorder: Relations with Child's Age, Gender, and Behaviour Problems. J. P. W. Maljaars^{*1}, G. Lambrechts², H. Boonen¹, K. Van Leeuwen¹ and I. Noens¹, (1)University of Leuven (KU Leuven), (2)Parenting and Special Education Research Unit, University of Leuven (KU Leuven)

Background: Parents of children with ASD are confronted with specific challenges in raising their children. These challenges are partly due to the specific behavioural characteristics of children with ASD. Moreover, children with ASD have a greater risk for developing behaviour problems compared to children without ASD (e.g., Kanne & Mazurek, 2011). Parenting behaviour can function as a risk factor but also as a protective factor in the development of problem behaviour (Patterson et al., 1992). Currently, there is only little research focusing on concrete parenting behaviour in families of children with ASD.

Objectives: 1) to characterize parenting behaviour among mothers of children with ASD and to explore differences compared to mothers of children without ASD; 2) to study the relation between parenting behaviour and child's age and gender in both groups; 3) to examine whether and how parenting behaviour is related to externalizing and internalizing behaviour problems of the children.

Methods: In this study 552 families of a child with ASD are compared with a control group of

437 families with a child without ASD (age range: 6-18 years). The Parental Behaviour Scale-short version (PBS; Van Leeuwen & Vermulst, 2010) was used to measure general parenting behaviour (Positive Parenting, Discipline, Harsh Punishment, Material Rewarding, and Rules), in combination with additional subscales to measure specific parenting behaviour relevant to children with ASD (Stimulating the Development and Adapting the Environment; Lambrechts et al., 2011). The Strengths and Difficulties Questionnaire was administered to evaluate behaviour problems. The first four subscales were used, creating two composite scores for internalizing behaviour problems (emotional and peer items) and externalizing behaviour problems (conduct and hyperactivity items) (Goodman et al., 2010).

Results: MANOVAs with diagnosis, gender, and age (primary vs. secondary education) as factors showed that mothers of children with ASD exhibit different parenting behaviour in several domains compared to the control group. Mothers of children with ASD utilize less Rules and Discipline ($ps < .001$), and show more Positive Parenting ($p = .02$). They also stimulate the development of their child and adapt the environment more often than the control group ($ps < .001$). Gender effects are found for Discipline and Stimulating the Development ($ps < .01$), whereas age effects are present in the domains Positive Parenting and Adapting the Environment ($ps < .001$). In general, only weak correlations were found between behaviour problems and parenting behaviour. Different parenting behaviour patterns are seen for externalizing versus internalizing behaviour problems.

Conclusions: Results indicate that more specifically relevant parenting was seen in the group of mothers with a child with ASD, but also differences in general parenting behaviour were present. The correlation patterns between behaviour problems and parenting behaviour suggest the presence of coercive family processes for externalizing behaviour problems in both groups. Internalizing problems are related to autism specific parenting behaviour in the ASD group. Future studies using observational and longitudinal measures are needed to validate these findings. Overall, this study will provide suggestions to improve prevention and

intervention of behaviour problems by enhancing parenting skills.

103.007 Gaze Patterns During an Eye-Tracking Measure of Joint Attention in Typically Developing Children and Children with Autism Spectrum Disorder. M. R. Swanson* and M. Siller, *Hunter College of the City University of New York*

Background: Longitudinal research that followed children with ASD over time found that many children eventually acquired the ability to respond to an adults' pointing gesture (Sigman & Ruskin, 1999). Despite these increases in social responsiveness, it remains unclear whether deficits in spontaneous gaze following persist across the autism spectrum and age span. Modern eye-tracking technology may be ideally suited to evaluate spontaneous gaze following across the age span.

Objectives: The current eye-tracking study evaluates children's gaze patterns while viewing a dynamic paradigm that elicits spontaneous gaze following. We predict that children's gaze patterns differ between diagnostic groups and are associated with individual differences in social awareness (SRS social awareness scores).

Methods: The sample included 21 children with ASD ($M=7.3$ years, $SD=1.5$ years) and 24 typically developing children (TD group) ($M=6.8$ years, $SD=1.6$ years) from ethnically diverse backgrounds. The Social Responsiveness Scale (Constantino, 2002) was used to rule out ASD in typically developing children and the Autism Diagnostic Observation Schedules-General (ADOS-G; Lord et al., 2000) was used to confirm diagnoses in children with ASD. The samples were well matched on chronological age, gender (ASD, 18/3; TD, 20/4, M/F), and receptive language age (ASD $M=85.10$ months; TD $M=86.83$ months).

Children watched videos that displayed a model (Face AOI) who gazes at a series of targets (Target AOI) that appeared and disappeared in the four corners of the screen (congruent condition). Gaze patterns in the congruent condition were compared to a set of control stimuli where the model's gaze was not directed at the targets (incongruent condition) (Swanson, Serlin, Siller, 2012). Gaze allocation to the Face and Target was evaluated based on total fixation

duration. To quantify 'sticky attention' to non-social stimuli, we also evaluated the duration of children's first fixation to the Target.

Results: Results did not reveal significant group differences in children's overall gaze allocation to the Target and Face AOI. However, findings showed significant group differences in the duration of children's first fixation to the Target AOI, $F=5.51$, $p<.05$. When both groups were combined, parent report measures of children's social awareness reliably predicted patterns of fixation duration to the Target ($F=7.76$, $p<.01$) and Face AOIs ($F=3.96$, $p<.05$), but not first fixation duration to the Target ($F=1.96$, $p=.16$). That is, individuals with better social awareness abilities showed reliable differences in fixation duration between the congruent and incongruent condition, while individuals with greater social disability showed indistinguishable fixation durations across both conditions.

Conclusions: Key findings from this research showed that quantitative individual differences in visual fixation were predicted by continuous measures of social abilities and impairment, but not children's diagnostic classifications. However, a qualitative measure of social salience (first fixation duration) did differ significantly between the two groups. This finding points to future directions for endophenotype research. By definition, endophenotypes aspire to be 'elementary' and closely related to the underlying neural circuitry of ASD. As a consequence, clinical measures used to validate candidate endophenotypes may be more successful if they capture a specific behavioral dimension of ASD rather than global diagnostic classifications.

Epidemiology Program

104 Epidemiology

This session provides results on the prevalence of ASD in at-risk groups, findings on prenatal and post-natal environmental exposures, results of detection programs, and issues of case definition in population based studies.

104.001 The ASD Phenotype in Neurofibromatosis Type 1: Evidence From a Two-Phase Population-Based Epidemiological Study. S. Garg¹, K. Leadbitter^{*1}, R. Emsley¹, A. Lehtonen², D. Trump², G. Evans², S. M. Huson² and J. Green¹, (1)University of Manchester,

(2)Central Manchester University Hospitals NHS Foundation Trust

Background: Neurofibromatosis Type 1 (NF1) is a common autosomal dominant disorder (birth incidence > 1 in 2,700), caused by mutation on chromosome 17 (17q11.2), with a well elucidated neuro-pathological pathway involving the RASMapkinase intracellular signalling pathway. Although noted for somatic manifestations, the main morbidity from NF1 is actually in cognitive, social and behavioural difficulties. Characterisation of the behavioural phenotype in NF1 has lacked well-designed epidemiological studies on representative samples, with previous studies on clinic-referral populations.

Objectives: To estimate the population prevalence of Autism Spectrum Disorders (ASD) in NF1 using rigorous methodology.

Methods: A two-phase population-based design using standardised assessment. In a **phase 1 screening stage** all parents of children aged 4-16 from a whole population NF1 Genetics Register in the North-West of England were invited to participate. 109/207 (53%) completed the Social Responsiveness Scale (SRS) to estimate autism symptoms, along with other questionnaire measures. Invitation to the **Phase 2 in-depth phenotyping stage** was stratified by random number generation of cases within three SRS groups. We assessed 97% of the clinical-range SRS scorers (T scores >75); 72% of the subclinical scorers (T score 60-75); and 31% of the normal-range scorers (T score <60). The Autism Diagnostic Interview-Revised (ADI-R), the Autism Diagnostic Observation Schedule (ADOS-G) and the Verbal IQ items of the Wechsler Abbreviated Scale of Intelligence (WASI) were delivered by experienced administrators. High inter-rater reliability on ADOS scores was confirmed on 20% of the sample. Collaborative Program of Excellence in Autism (CPEA) criteria (Lainhart et al. 2006) were used to combine IQ, ADI-R and ADOS-G scores into ASD and 'Broad ASD' (partial features) categories. Statistical analysis used weighting of this phase 2 CPEA categorisation in order to estimate the representative population prevalence of ASD and Broad ASD.

Results: Responders and non-responders in both phases did not differ on key characteristics. In **Phase 1** 28.7% (31/109) of children scored in the severe, clinical autism range on the SRS (T score >75); 29.9% (29/109) in the mild to moderate range (T score 60-75) and 44% of children in the normal range (T score <60). In **Phase 2**, 29.8% of the sample met CPEA ASD criteria and a further 27.6% showed 'Broad ASD' with partial features. Mean verbal IQ was 95.56(16.61) and did not differ across these groups. 20/47 (42.5%) met ADOS-R ASD criteria and 12/47 (25.5%) met ASD criteria on 3 ADI-R domains. ASD was not associated with the extent of physical illness, age, SES, or familial inheritance of NF1.

Weighting these results by the probability of responding to phase 1 gives a whole-population prevalence for ASD of 24.9% (95%CI 13.1%, 42.1%) and for Broad ASD of 20.8% (95%CI: 10.0%, 38.1%).

Conclusions: This two-phase epidemiological study yields an ASD population prevalence in NF1 of 25%, with a further 21% showing "broad ASD" with partial features. Because the pathogenesis of NF1 is known in detail and there are interventions theoretically impacting on the pathway, this makes NF1 an important single gene model of autism with considerable potential for future research in illuminating the nature of the disorder.

104.002 Association Between ART Conception and Autism in California 1997-2007. C. Fountain^{*1}, Y. Zhang², D. Kissin², L. A. Schieve³, D. Jamieson², C. E. Rice³ and P. S. Bearman⁴, (1)*Fordham University*, (2)*Centers for Disease Control and Prevention*, (3)*National Center on Birth Defects and Developmental Disabilities*, (4)*Columbia University*

Background: The estimated US prevalence of autism spectrum disorders has increased rapidly over the past two decades and is now estimated as 1 in 88 children. During the same period, the use of assisted reproductive technology (ART) has increased rapidly. ART and autism have many common correlates including older parental age, higher parental education, multiple births, preterm delivery, low birth weight, and pregnancy and labor complications. Few studies have investigated the relationship between ART and autism, and existing results are mixed and inconclusive. Given the increasing use of ART and

the uncertain etiology of autism it is important to know whether these phenomena are associated.

Objectives: To assess the association between ART and diagnosed Autistic Disorder in a population-based sample of US births using the largest existing source of information on ART and autism.

Methods: We linked records from the California Birth Master Files for 1997-2007, the California Department of Developmental Services (DDS) autism caseload for 1997-2011, and the CDC's National ART Surveillance System for live births in 1997-2007. Of 5,926,251 births, 48,865 infants (0.8%) were conceived through ART and 32,922 (0.6%) were later diagnosed with autism and enrolled with the DDS. We calculated autism risk for ART and non-ART births. To reduce the likelihood of ascertainment bias for autism diagnosis, we created an analytic subsample restricted to births to women age >20 years who had obtained a high school diploma or higher education, adequate prenatal care, and whose prenatal care and delivery were covered by a non-public payment source. We estimated crude and adjusted Hazard Risk Ratios for the subsample, considering several demographic and pregnancy-related factors as potential confounders. We also estimated adjusted Hazard Risk Ratios stratified by infant sex, parental age, maternal education, and parity. Finally, nested adjusted models were estimated to examine potential causal pathways for the ART-autism association.

Results: In the full population, the prevalence of diagnosed autism is twice as high for ART as non-ART births (crude HRR=2.3 [2.1-2.5]). The association is diminished in the analytic subsample (crude HRR=1.8 [1.6-1.9]); adjusting for demographics, maternal age, and parity further attenuates the association although it remains significant (HRR=1.4 [1.3-1.5]). Stratified adjusted analyses show significantly elevated HRRs in all subgroups, with a significantly stronger effect among children born to mothers <35 years than >35 years of age (adjusted HRR 1.7 [1.5-2.0] vs. 1.4 [1.2-1.5]). However, after inclusion of adverse prenatal and perinatal outcomes potentially in the causal pathways (multiple birth, preterm, small for gestational age, maternal diabetes and hypertension, and cesarean delivery) the

association was reduced to the null for both maternal age groups.

Conclusions: Findings from this analysis suggest a potential association between ART and autism. However, it is uncertain if the pathway for the observed association is a direct effect of the ART procedure: when adverse prenatal and perinatal factors are accounted for, the independent association is reduced to null.

104.003 Prenatal Exposure to Perfluorinated Compounds (PFC) and Autism Spectrum Disorders: Results From the Early Markers for Autism Study. V. Yau*¹, C. Yoshida¹, R. Hansen², M. Kharrazi³, A. Calafat⁴, G. C. Windham⁵ and L. A. Croen⁶, (1)*Kaiser Permanente*, (2)*University of California, Davis*, (3)*California Department of Public Health*, (4)*Centers for Disease Control and Prevention*, (5)*California Dept of Public Health*, (6)*Kaiser Permanente Division of Research*

Background: Perfluorinated Compounds (PFC's) are chemically stable, persistent chemicals widely used in industrial applications as well as consumer products. Several have been identified as developmental and immune system toxicants. Greater than 98% of the US population had detectable serum levels of several classes of PFC's in a NHANES survey (2003-2004). However, no studies have examined the potential link between prenatal PFC exposure and risk of autism.

Objectives: To determine the association between PFC concentrations in maternal blood samples collected during mid-pregnancy and risk of autism spectrum disorders (ASD's) in the child.

Methods: The study population came from the Early Markers for Autism (EMA) study, a population-based nested case-control study of children born from 2000 to 2003 in Southern California. Children diagnosed with an ASD (N = 430) or a developmental delay but not autism (DD, N = 328) were identified from the Department of Developmental Services (DDS). Controls (N=439) were randomly sampled from birth certificate files and matched to ASD cases on gender, birth month, and birth year. ASD and DD diagnoses were validated based on review of DDS medical records. Following expert review, 136 children were reclassified from the DD group to the ASD group (final ASD N=566).

All mothers were participants in California's prenatal expanded alpha-fetoprotein screening program. Maternal serum samples were collected at 15-19 weeks gestational age. After routine prenatal screening testing was complete, left-over samples were stored frozen and later analyzed for concentrations of 8 PFC's (PFOA, PFOS, PFNA, PFHxS, PFDEA, PFOSA, Et-PFOA, and Me-PFOA) using a high-performance liquid chromatography-tandem mass spectrometry device and an on-line solid phase extraction method. Exposure levels in the controls were used to develop quartile cutoff points. Unconditional logistic regression was used to model the odds ratios comparing prenatal exposure in cases vs. controls. Regression models were adjusted for demographic variables as well as matching variables.

Results: PFC median concentrations (ng/mL) in this population were lower than those reported in the NHANES populations (PFOS Medians: NHANES 1999-2000 = 30.2, NHANES 2003-2004 = 21.2, EMA = 17.90; PFOA Medians: NHANES 1999-2000 = 5.1, NHANES 2003-2004 = 4.1, EMA = 3.60).

PFDeA and PFOSA concentrations were mainly below limits of detection, consistent with NHANES results (PFDeA = 83.3% <LOD, PFOSA = 75.4% <LOD). Preliminary analyses indicated that PFOA concentrations were negatively correlated with odds of developing ASD (OR, upper quartile vs. lower quartile: 0.64, 95% CI [0.42, 0.97], p-value = 0.033). Risk of ASD was not significantly associated with prenatal exposure to other PFC's, though further analysis is necessary.

Conclusions: Preliminary results indicate that concentrations of PFC's during pregnancy in the EMA population were similar to, though somewhat lower than, the NHANES population. Concentrations of PFC's varied widely, both by demographic and diagnostic groups. Exploration of main effects as well as differing effects of PFC's by subgroups of demographic variables will be further explored in this large, diverse population.

104.004 Maternal Depression, Antidepressant Use During Pregnancy, and Offspring Autism Spectrum Disorders: Population-Based Study. D. Rai*¹, B. K. Lee², C. Dalman¹, J. Golding³, G. Lewis³ and C. Magnusson¹, (1)*Karolinska Institutet*, (2)*Drexel University School of Public Health*, (3)*University of Bristol*

Background: Recent research has raised the possibility of a higher risk of autism spectrum disorder (ASD) in offspring of mothers prescribed selective serotonin reuptake inhibitor (SSRI) antidepressants during pregnancy. Further research is required to verify and provide further insights into this finding.

Objectives: To study i) the association between parental depression and maternal antidepressant use during pregnancy with offspring ASD; ii) whether associations between antidepressant use and ASD are unique to SSRIs; and iii) whether the associations are similar for ASDs with or without intellectual disability (ID).

Methods: A case-control record-linkage study nested within a cohort of all individuals 0-17 years living in Stockholm County between 2001 to 2007 (n=589,114), using data on parental depression and other characteristics prospectively recorded before the birth of the child. Maternal antidepressant data, recorded at the first antenatal interview was available for children born 1995 onwards. ASDs (n=4429 in complete sample, n=1679 with antidepressant use data) were identified using multisource case-ascertainment.

Results: A maternal history of depression was associated with an increased risk of offspring ASD but in the smaller sample with available data, this association appeared to be confined to women reporting antidepressant use during pregnancy (adjusted OR=3.34, 95% CI (1.50-7.47), p<0.01). The associations were observable in mothers using SSRI as well as non-SSRI antidepressants, and all associations seemed to be driven by heightened risks in cases of ASD without ID, there being no increase in risk for ASD with ID.

Conclusions: Although it is impossible to rule out confounding by indication (i.e. depression severe enough to require antidepressants during pregnancy leading to ASD), this study adds to the evidence suggesting a potential association between in-utero exposure to antidepressants and ASD, and highlights that the associations are not unique to SSRI's and are largely confined to cases of ASD without intellectual disability.

104.005 Role of Vegetables and Seafood Consumption in Blood Manganese Concentrations in Jamaican Children with and without Autism Spectrum Disorders. M. H. Rahbar*¹, M. Samms-Vaughan², A. S. Dickerson³, K. A. Loveland⁴, M. Ardjomand-Hessabi¹, J. Bressler³, S. Shakespeare-Pellington², M. L. Grove³, D. A. Pearson⁴ and E. Boerwinkle³, (1)*The University of Texas Health Science Center at Houston*, (2)*The University of the West Indies*, (3)*The University of Texas School of Public Health at Houston*, (4)*University of Texas Medical School*

Background:

Manganese is a trace element essential for human health and development. The Agency for Toxic Substances and Disease Registry recommends blood manganese concentrations (BMnCs) between 4-15 µg/L. Elevated and low levels of manganese in blood can adversely affect the nervous system, potentially leading to neurobehavioral impairment. Autism Spectrum Disorders (ASDs) are complicated neurodevelopmental and behavioral disorders that manifest in early childhood and continue into later life. Limited but conflicting data have been reported regarding the potential role of manganese in the development of ASD which suggests the need for additional studies.

Objectives:

To investigate the association between BMnCs and ASD in Jamaican children, and to assess the role of vegetables and seafood consumption in BMnCs among these children.

Methods:

The Jamaican Autism study is a NIH-supported age- and sex-matched case-control study that started recruitment in December 2009 to investigate whether environmental exposures to mercury, lead, arsenic, manganese, and cadmium have a role in the onset of autism. We administered the Autism Diagnostic Observation Schedule and the Autism Diagnostic Interview-Revised to children, 2-8 years of age, from the Jamaican Autism Database at the University of the West Indies. For each case, we identified an age- and sex- matched typically developing child as a control; using the Social Communication Questionnaire to insure that controls did not have

significant ASD symptomatology. We also administered a pre-tested questionnaire to assess demographic and socioeconomic information, parental education levels, medical history of children, and potential exposure to manganese through food, with a particular focus on the types and amount of vegetables and seafood consumed by children. Finally, we collected 2 mL of whole blood from each child, which was analyzed for manganese levels. Using a General Linear Model, we assessed the association of BMnCs with ASD status and sources of exposure to manganese based on data from the available 65 matched pairs.

Results:

In our samples, 86.2% of children were male with a mean age of about 65 months. The cases and controls were 96.9% and 98.5% Afro-Caribbean, respectively. The mean BMnC for children who ate fried plantains was significantly higher than those who did not, (11.3 vs. 8.6 μ g/L; $P=0.05$). In contrast, the mean BMnC for children who ate shellfish was significantly lower than that of children who did not report consuming shellfish, (6.2 vs. 11.0 μ g/L; $P=0.04$). In univariable analysis, we did not find a significant association between BMnCs and ASD, (10.8 μ g/L for both cases and controls; $P = 0.95$). After controlling for consumption of tuna, shellfish, fried plantains, ackee, and whole wheat bread, there was no significant association between BMnCs and ASD status, (11.0 for cases vs. 10.6 μ g/L for controls; $P=0.61$). Overall, 4.6% of children in our sample had elevated BMnCs (i.e., >15 μ g/L) of whom 83% ate fried plantains. However, none of the children in our samples exhibited manganese deficiency (<4 μ g/L).

Conclusions:

Our findings do not support an association between BMnCs and ASD in Jamaican children. However, children who ate fried plantains appear to be at a higher risk of having an elevated BMnC.

104.006 Insecticides and Autism: Overview and New Results From the Charge Study. I. Hertz-Picciotto^{*1}, L. Delwiche², F. Tassone¹, D. Bennett², D. J. Tancredi³, R. Hansen⁴, S. Ozonoff¹ and I. N. Pessah¹, (1)UC Davis M.I.N.D. Institute, (2)UC Davis, (3)UC Davis School of

Background: Insecticides are designed to damage living organisms, often by targeting the CNS. Several recent studies have provided evidence of a link between specific classes of pesticides and the risk for autism or for symptoms of pervasive developmental disorders (PDD). These used objective measures of exposure: one linked commercial applications of organochlorine, pyrethroid, and other pesticides from a statewide database to residences during pregnancy; a second attempted to replicate those findings in a sample of cases and controls with more detailed confounding information; a third measured urinary metabolites of organophosphates during pregnancy and followed the children, obtaining the PDD measures through the Child Behavior Checklist.

Objectives: 1) To examine the relationship of autism spectrum disorder (ASD) risk with household applications of insecticide products and specific active ingredients in those formulations. 2) To evaluate evidence for an interaction between pyrethroid exposures and MAOA genotype.

Methods: Participants (n=783) were enrolled in the Childhood Autism Risks from Genes and Environment (CHARGE) study beginning in 2003. ASD was confirmed on the ADOS and ADI-R. Controls were recruited from State birth files, using a stratified random sample matched on age, sex, and broad geographic area, and were considered typically developing (TD) if they scored higher than 2 SD below the mean on Mullen's Scales of Early Learning and Vineland Adaptive Behavior Scales, and below 15 on the Social Communications Questionnaire. Exposures to household products were collected through an extensive interview that obtained product type, use and brand, and associated time periods from preconception through pregnancy and early childhood. Insecticides were searched in online databases containing active ingredients by brand, type, and date to assign specific chemical exposures. Standard PCR was used for genotyping the variable number tandem repeats in the promoter region of the X-linked MAOA gene.

Results: Parents of ASD children were more likely than those of controls to report applications of insecticide sprays and foggers in the preconception and pregnancy period, and the products they used were more likely to contain pyrethroids (multivariate adjusted Odds Ratio, aOR=1.88 (95% confidence interval (CI), 1.21, 2.94)). Repeated applications (6 or more months during pregnancy) conferred especially high risk (aOR=3.47, 95% CI=1.48, 8.11). Boys carrying four tandem repeats in the MAOA promoter locus, were at exceptionally high risk (nearly five-fold) if pyrethroids were used. Products containing less toxic pyrethrins carried lower risks, and results were robust to various sensitivity analyses.

Conclusions: Reporting accuracy could differ for mothers of ASD versus unaffected children, but the synergistic relationship for pyrethroid use and MAOA genotype is incompatible with this explanation. Moreover, participants reported products they used, not exposures: the latter were determined by linkage of product type, brand, and year of use with databases providing active ingredients; these often changed over time. Evidence presented here suggests the pyrethroid class of insecticides comprise a modifiable environmental factor that may increase ASD risk, particularly in genetically susceptible individuals, but replication in a prospective setting should be sought.

104.007 Early Identification of Autism in Spain: Exploring Diverse Possibilities with the MCHAT. P. Garcia Primo^{*1}, R. Canal-Bedia¹, M. Magán Maganto¹, M. V. Martín Cilleros¹, B. Esteban Manjón¹, I. Guerra Juanes¹, A. Zermeño Perez¹, M. M. Herráez¹ and M. Posada², (1)University of Salamanca, (2)Carlos III National Institute of Health

Background: The AAP has recommended autism screening for all children at 18 and 24 months (AAP, 2007). The MCHAT is the most well-studied, validated and useful screening tool for autism at early ages (Robins, Fein, Barton & Green, 2001) but more empirical data is needed. It has been confirmed the difficulties of the MCHAT in distinguishing ASDs from other DDs (Ventola et al 2007, Canal et al 2011) at the screening level. High rate of false positives (FP) can create unnecessary stress for parents and lead to expensive and time consuming diagnostic evaluations. It also has been suggested that MCHAT is better at detecting autism in children

aged 24 months than those aged 18 months (Pandey 2008). Therefore best age to instigate screening neither added value of screening at two time points are still conclusive.

Objectives: This study seeks to investigate further the possibilities of the use of the MCHAT as an efficient yet effective screening instrument to detect autism in community and at-risk populations. The main focus is to test and discuss the different options to administer the MCHAT identifying the most operational items and best cut-offs in assorted samples in order to determine if the measure needs to be adapted accordingly.

Methods: Parents of 18 months and/or 24 months aged children were asked to fill in the Spanish version of the MCHAT (Canal, 2011) at the outpatient health services (compulsory vaccination and well-child check-up programs respectively) in several health areas in Spain (Low Risk -LR-). For validation purposes, parents of children referred to early intervention services were also asked to fill out the MCHAT questionnaires when the child was aged 16-36 months old (High Risk -HR-). Analysis and data collection are ongoing. MCHAT data has been gathered from 7835 children: (7835 LR) 5270 at 18 months and 4819 at 24 months, including a subset of 2254 children screened 2 times and from 104 HR-children. Additional information on ADOS, V/NV-IQ and clinical diagnosis from LR-children with MCHAT positive results and from all HR children (regardless screening results) has been likewise recorded. MCHAT Best7 (Robins, IMFAR 2010&2011), MCHAT-R (Robins, IMFAR2011) and new potential scoring algorithms of the MCHAT, based on item analysis were examined in the different samples for psychometric properties.

Results: The preliminary findings suggests that the MCHAT used in HR population does not have the same sensitivity and specificity as noted in the general population regardless the scoring or algorithm used. Sen. & Sp are also different at 18 vs 24 m.o. (.57&0.90 Vs 0.71&0.92 respectively) within the same re-screened children. Aspects of pointing, joint attention and social reference on the MCHAT (ITEMS 6,7,9,23) seemed to be indicative of children subsequently diagnosed with ASD more than children with other DDs.

Conclusions: Efforts must continue to reduce the false positive rate without significantly increasing the number of missed cases. The analysis of the variability of the samples characteristics will determine the reliability of the findings. Improvement in screening will benefit parents, children and very likely health and early intervention resources.

104.008 Using Standardized Diagnostic Instruments to Classify Children with an Autism Spectrum Disorder in the Study to Explore Early Development. L. D. Wiggins*¹, A. M. Reynolds², C. E. Rice³, E. Moody⁴, P. Bernal⁵, L. Blaskey⁶, S. Rosenberg⁷, L. C. Lee⁸ and S. E. Levy⁶, (1)*Centers for Disease Control and Prevention*, (2)*University of Colorado Denver*, (3)*National Center on Birth Defects and Developmental Disabilities*, (4)*University of Colorado, Denver*, (5)*Kaiser Permanente*, (6)*Children's Hospital of Philadelphia*, (7)*University of Colorado*, (8)*Johns Hopkins Bloomberg School of Public Health*

Background: The Study to Explore Early Development (SEED) is a case-control study funded by the Centers for Disease Control and Prevention (CDC) to examine autism spectrum disorder (ASD) phenotypes and etiologies. One of SEED's greatest strengths is use of gold standard diagnostic instruments – the Autism Diagnostic Interview Revised (ADI-R) and Autism Diagnostic Observation Schedule (ADOS) – as well as a combination of other factors, such as mental age of the child, to classify children with ASD.

Objectives: The objectives of this analysis were to (1) describe how children were classified in SEED and (2) examine the psychometric properties of SEED ASD criteria, ADOS alone, ADI-R alone, and ADOS plus ADI-R without consideration of other factors (i.e., ADOS/ADI-R standard criteria).

Methods: Children 2-5 years old were ascertained through birth certificate records and multiple sources that serve children with developmental problems. All children were screened for ASD upon enrollment. Children without a prior ASD diagnosis who had little risk noted on the ASD screen received a cognitive assessment only. Children with a prior ASD diagnosis or who had risk noted on the ASD screen received the ADI-R, ADOS, cognitive assessment, and adaptive assessment. After the developmental evaluation,

all children were classified into one of the following groups: ASD, developmental delay or disorder (DD), population comparison (POP, identified from birth certificate records), or Possible ASD. Children classified as DD, POP, or Possible ASD were further divided into one of numerous subgroups. SEED ASD criteria took into account numerous factors, including ascertainment source, results of the ADI-R and ADOS, rules for resolving discordance between the ADI-R and ADOS, mental age of the child, and – in some instances – clinical judgment.

Results: A total of 2,732 children were enrolled in SEED and completed a clinic visit. SEED final classifications for these children were ASD (N=703), DD (N=999), POP (N=906), and Possible ASD (N=124). There were 1,063 children who received the ADI-R, ADOS, and cognitive assessment and had clinical judgment noted. Of these, 921 had a mental age of at least 24 months and 142 had a mental age less than 24 months. ADI-R and ADOS results were discrepant in 22.8% of this sample.

The ADOS yielded the highest sensitivity but the lowest specificity than any other classification scheme. The sensitivity and specificity of other classification schemes were relatively comparable. ADOS/ADI-R standard criteria missed 62 more children with certain ASD (defined by clinical judgment) than SEED ASD criteria. Likewise, SEED ASD criteria classified 27 more children with uncertain ASD (defined by clinical judgment) than ADOS plus ADI-R standard criteria.

Conclusions: These findings support the utility of SEED ASD criteria in population-based research. Three major advantages of SEED ASD criteria are: (1) a method for resolving discordance between the ADOS and ADI-R, (2) a method for classifying children with a mental age less than 24 months, and (3) detailed classifications and sub-classifications that allow phenotypic exploration. Future research should explore whether SEED classifications identify children with different phenotypes that can be used as important outcomes in SEED.

Animal Models Program
105 Animal Models of Autism

105.001 1 Transgenerational Actions of Endocrine Disrupting Compounds On Brain and Behavior: Implications for Autism. E. Rissman*, *University of Virginia School of Medicine*

Background: Prevalence of Autism Spectrum Disorder (ASD) has increased dramatically over the past few decades. According to the CDC, the incidence of ASD in 2000 was 1:150; now the level is 1:88. While candidate gene mutations, SNPs and CNVs have been discovered, no one gene accounts for more than 1% of ASD. Our lab is asking how environmental factors, particularly via epigenetic regulation of gene transcription, may contribute to changes in social behavior.

Exposure to endocrine disrupting compounds (EDC) is widespread through many sources including; food can linings, plastic products, cosmetics and paper to name a few. The actions of these compounds

Objectives: Our goal was to assess effects of Bisphenol A on a set of social behavior and expression of neural genes over the course of 3-4 generations in laboratory mice.

Methods: We exposed mice to BPA only during gestation. We employed doses of BPA that produce blood levels comparable to those found in humans; to date we have used three different doses. Our behavioral data illustrate the non-monotonic effects of BPA. To ask if the actions of BPA are transgenerational we compared gene expression and behavior in mice from the first, second, third, and/or fourth generations.

Results: Juveniles exposed to in the first generation displayed fewer social interactions as compared with control mice, whereas in later generations (F₃ and F₄), the effect of BPA was to increase general activity. Brains from embryonic day 18.5 had lower gene transcript levels for several estrogen receptors, oxytocin and vasopressin as compared to controls; decreased vasopressin mRNA persisted into the F₄ generation, at which time oxytocin expression was also reduced but only in males.

Conclusions: Thus, exposure to a low dose of BPA, only during gestation, has immediate and long lasting, trans-generational, effects on mRNA in brain and social behaviors. These heritable effects of exposure to an endocrine disrupting

compound have implications for complex diseases, which are likely the result of gene-environment interactions.

105.002 2 Environmental Impacts On the Brain and Behavior. H. Patisaul*, *North Carolina State University*

Background: Although it has long been suspected that environmental factors such as chemical contaminants, dietary components, infection or even maternal stress might contribute to autism, there is a paucity of data demonstrating a clear link. However, a wide range of animal studies, across a diverse array of species, have found that exposure to endocrine disruptors during critical periods of development can induce behavioral changes such as increased anxiety, hyperactivity, and altered social behavior. This talk will summarize data from our lab and others demonstrating that exposure to chemicals during critical periods of developmental can induce behavioral changes consistent with components of autism spectrum disorders (ASDs). Associated neural changes which may help identify the underlying mechanisms for these behavioral changes will also be highlighted.

Objectives: The goal of our ongoing studies is to explore the behavioral and neural impacts of developmental exposure to endocrine disrupting compounds and identify potential modifying or mitigating factors such as diet.

Methods: Using a wide variety of behavioral testing paradigms (elevated plus maze and similar) and rodent species, we are assessing how early life exposure to endocrine disruptors, specifically, the plastics component Bisphenol A (BPA), soy phytoestrogens, and a newly discovered fire retardant, Firemaster 550 (FM 550), alter social and affective behaviors across the lifespan. To understand the mechanisms by which these behavioral effects are conferred, we use a variety of techniques including immunohistochemistry and RT-PCR arrays to identify associated changes in the brain. Our primary focus is on limbic structures important for modulating social and affective behaviors, such as the amygdala and paraventricular nucleus (PVN).

Results: Rats of both sexes, perinatally exposed to a human-relevant dose of BPA were more anxious in adolescence and adulthood but these effects were mitigated by a soy-rich diet, suggesting that

dietary factors may be protective. In the amygdala, expression levels of the beta form of the estrogen receptor (ESR2; $p < 0.002$) and a melanocortin receptor (MC4R; $p < 0.01$) were downregulated by BPA exposure. These genes are required for oxytocin, release suggesting that the oxytocin/vasopressin system, which is well recognized to be important for social behavior and bonding, may be vulnerable to chemical insult. In the monogamous prairie vole, BPA exposed females were hyperactive, an effect consistent with what has been reported in young girls. Emerging data from our lab also reveals that FM 550 alters anxiety levels in rats of both sexes.

Conclusions: Collectively, these data support the hypothesis that environmental exposures during critical windows of development may contribute to behavioral characteristics contained within the autism spectrum. The consistency and reproducibility of behavioral effects across species is particularly strong supporting evidence for the idea that chemical exposures may contribute to autism risk. Strategies for utilizing this data to better understand how endocrine disruptors and other environmental contaminants may be contributing to autism and related disorders will also be discussed.

105.003 3 A Nonhuman Primate Model of Maternal Immune Activation. M. D. Bauman*, *UC Davis*

Background: Maternal infection during pregnancy is associated with an increased risk of having a child later develop a neurodevelopmental disorder, such as autism or schizophrenia. In a mouse model of maternal immune activation (MIA), administration of the viral mimic dsRNA poly(I:C) to pregnant dams results in offspring with increased anxiety and repetitive behaviors as well as deficits in social interaction and communication.

Objectives: To further evaluate this risk factor, we have adapted the rodent polyI:C model for use in the nonhuman primate.

Methods: A modified form of poly(I:C) was delivered to pregnant rhesus monkeys (*Macaca mulatta*) at the end of either the first or second trimester. A separate control group of pregnant rhesus monkeys received saline injections at these time points. Behavioral development of the MIA-exposed macaque offspring was then

systematically evaluated for the first 4 years of life.

Results: MIA-exposed macaque offspring demonstrate atypical repetitive behaviors, vocalizations and social interactions.

Conclusions: MIA in the nonhuman primate model was associated with alterations in brain, behavior and immunological development that resemble features of human neurodevelopmental disorders.

105.004 4 Identification of Maternal Antibody Targets in Autism: Autism-Specific Maternal Autoantibodies Are Directed Against Critical Proteins in the Developing Brain. J. Van de Water*, *The M.I.N.D. Institute, University of California, Davis*

Background: Previous observations of fetal-brain reactive maternal IgG antibodies in a subset of mothers of children with autism spectrum disorder (ASD), and an association between presence of these antibodies and severe behavioral manifestations led us to undertake identification of the protein targets of these antibodies. Fetal exposure during gestation to brain-reactive maternal IgG may be the underlying cause of the behavioral symptoms noted in some ASD cases and unraveling the molecular interactions between these antibodies and their targets may open new avenues for treatment and prevention.

Objectives: The focus of this project was to identify the molecular targets of ASD associated, fetal-brain reactive maternal IgG antibodies.

Methods: A protein extract derived from fetal Rhesus macaque (152 day gestation) was fractionated by molecular weight and individual fractions were probed with plasma from mothers of children with ASD. Fractions containing antigenic proteins were subjected to duplicate 2-dimensional gel electrophoresis, with one gel being transferred to nitrocellulose and probed with maternal plasma to identify antigen location, and the other used for spot picking and tandem MS/MS analysis. Verification of MS results was carried out using commercially available purified or recombinant proteins, and further confirmed using blocking studies. Reactivity to the identified protein antigens was determined in a sample of

246 mothers of children with ASD and 149 mothers of typically developing children.

Results: Seven proteins were identified and confirmed to be the antigenic targets of ASD-associated maternal IgG. The 37kDa antigen is an essential metabolic enzyme with well characterized functions in neurogenesis. The 44kDa antigen is an enzyme known to regulate post-synaptic targeting. The 39kDa protein has an important role in late embryogenesis. Two proteins were identified as 73kDa antigens – one that is critical for neuronal growth cone collapse upon and the other that functions as a chaperone for several heat-shock proteins and mediates neuritogenesis. Confirmed reactivity to the 37kDa and both of the 73kDa proteins is observed exclusively among mothers of children with ASD with a prevalence of approximately 8%, yielding an odds ratio of 24.2 (95% CI: 45-405). Their children displayed significantly elevated stereotypical behaviors compared to ASD children from mothers lacking these antibodies.

Conclusions: Maternal IgG reactivity to the protein antigens identified in this study constitutes the most significant biomarker of ASD risk identified to date. In our study sample, reactivity to the 37kDa and 73kDa proteins was observed in approximately 8% of mothers of children with ASD and absent in mothers of typically developing children yielding a highly significant association with ASD ($p=0.00001$). Furthermore, previous findings from our group and others indicate that such maternal antibodies are often present during pregnancy, supporting the hypothesis that they could play a causal role in precipitating the behavioral outcomes noted in some cases of ASD.

105.005 5 An Animal Model for the Fetal Valproate Syndrome. F. Bertelsen^{*1}, A. Møller¹, A. M. Landau¹, P. Weikop², A. Sabers³ and J. Scheel-Krüger⁴, (1)*PET-centre, Aarhus University Hospital*, (2)*Laboratory of Neuropsychiatry, Psychiatric Centre Copenhagen*, (3)*The Epilepsy Clinic, Department of Neurology, Rigshospitalet*, (4)*Center of Functionally Integrative Neuroscience, Aarhus University*

Background: In the human clinic the fetal valproate syndrome is characterized by somatic malformations and cognitive dysfunctions, which include the autistic spectrum disorders.

Objectives: The objective of this study is to establish a novel animal model for autism induced by chronic, prenatal administration of the antiepileptic drug valproate (VPA) to pregnant rats.

Methods: Eighteen pregnant rats were exposed to daily clinically relevant doses of VPA or saline from the 12th day of pregnancy until birth. Neuropathological changes in the offspring were evaluated by stereology and presence of biomarkers in the prefrontal cortex, hippocampus and striatum. Behavioral changes relevant to autism were also investigated.

Results: We have found a significant increase in the number of neocortical cells in the offspring of the VPA rats compared to controls. Serotonin levels in the striatum of the VPA rats were significantly reduced compared to controls. Furthermore the male juvenile play behavior of VPA rats was reduced.

Conclusions: The combined approach of histology, biochemistry and behavioral studies is necessary in the characterization and development of a novel rodent model of autism. Translational studies using this model may result in a better understanding of the developmental changes occurring during pregnancy and leading to autism in the human condition. A valid animal model is the first step in the testing of new drug candidates of interest for the pharmacological treatment of autism. This is of particular importance since the deficits in social behavior in autism are severely invalidating and no pharmacological compounds are currently available for the improvement or treatment of the devastating core behavioral symptoms.

105.006 6 Btbrt+Tf/J Mice Exhibit an Inflammatory Macrophage Cytokine Profile with Associations to Repetitive Grooming Behavior. C. E. Onore^{*1}, M. Careaga¹, B. Babineau², J. Schwartz¹, J. Crawley³, R. F. Berman¹ and P. Ashwood¹, (1)*The M.I.N.D. Institute, University of California, Davis*, (2)*San Francisco School of Medicine*, (3)*M.I.N.D. Institute, University of California, Davis*

Background: Although autism is a behaviorally defined disorder, systemic associations are also noted with a number of studies reporting atypical myeloid cell phenotype and function including increased pro-inflammatory cytokine production.

Recent characterization of the BTBRT^{tf}/J (BTBR) inbred mouse strain revealed several behavioral characteristics including social deficits, repetitive behavior, and atypical vocalizations which may be relevant to autism. We therefore hypothesized that BTBR mice may exhibit immune abnormalities similar to those observed in children with autism when compared to social C57BL/6J (C57) mice.

Objectives: The objectives of this study were to characterize the immune profile of BTBR macrophages and associations with autism relevant behaviors including sociability and repetitive grooming.

Methods: All procedures were performed with approval by the University of California, Davis Institutional Animal Care and Use Committee in accordance with the guidelines provided by the National Institutes of Health for the scientific treatment of animals. C57 mice n=9, and BTBR n=7 mice were tested for social preference using the automated three-chambered social approach apparatus, and scored for self-grooming behavior. Post behavioral testing, mice were sacrificed and bone-marrow derived macrophages were generated. Macrophages were incubated for 24hr in growth media alone, 10 ng/ml LPS, 1 ng/ml recombinant IL-4/10 ng/ml LPS, or 150 ng/ml recombinant IFN- γ /10 ng/ml LPS. Supernatants were analyzed by Milliplex® immunoassay

Results: BTBR produced higher levels of inflammatory cytokines as compared to C57 macrophages including increased MCP-1 (p=0.0164) without stimulation, and increased IL-6 (p=0.0003), MCP-1 (p=0.0002), and MIP-1 α (p=0.0002) and lower IL-10 (p=0.0003) after stimulation with LPS. After exposure to the IL-4/LPS (p=0.0003), BTBR macrophages produced significantly less IL-10 than C57 macrophages while levels of IL-6 (p=0.0052), MCP-1 (p=0.0115), and MIP-1 α (p=0.0021) were significantly higher. After exposure to IFN- γ /LPS, BTBR macrophages produced significantly less IL-12 (p40) (p=0.0002) than C57 macrophages, while levels of IL-6 (p=0.0021), MCP-1 (p=0.0002) remain higher. We further observed a positive correlation between time spent grooming, and production of MCP-1 (p=0.0583) and MIP-1 β (0.0583) in untreated BTBR macrophages, and

production of IL-6 (p=0.0333), and TNF- α (p=0.0167) after treatment with IFN-g/LPS.

Conclusions: BTBR mice display a trend to increased inflammatory cytokine production including IL-6, MCP-1 and MIP-1 α , and decreased production of the anti-inflammatory cytokine IL-10, suggesting a more inflammatory macrophage phenotype in asocial BTBR mice compared to the social C57 strain. In addition to this inflammatory phenotype, BTBR macrophages show a impaired ability to produce IL-10 in response to treatment with the M2 polarizing condition IL-4/LPS, and IL-12(p40) in response to the M1 polarizing condition IFN- γ /LPS, suggesting that macrophages fail to polarize correctly in response to M1 or M2 polarizing cytokine signals. We additionally observed positive association between increased inflammatory cytokine production and increased repetitive behavior, which may suggest a direct relationship between inflammatory phenotype and a behavioral phenotype that may have relevance to a core symptom of autism.

105.007 7 Characterization of Mood and Anxiety Phenotypes in a Mouse Model of *Pten* Haploinsufficiency. A. Clipperton-Allen and D. Page*, *The Scripps Research Institute*

Background: Haploinsufficiency for *PTEN*, which encodes a negative regulator of the PI3 kinase pathway, is a risk factor for autism spectrum disorder (ASD) and macrocephaly. Using a mouse model of *Pten* haploinsufficiency, we have previously found that mutant mice show deficits in social approach behaviour, as well as brain overgrowth.

Objectives: To further characterize behavioral changes in *Pten* haploinsufficient mice, we are testing these animals using an extensive phenotyping battery. We have a particular focus on behavioral assays that probe the serotonin pathway as a candidate neural system underlying these changes, given our previous finding that haploinsufficiency for serotonin transporter can modify phenotypes in *Pten* haploinsufficient mice.

Methods: Our behavioral phenotyping battery includes assays of mood and anxiety (tail suspension test and dark-light emergence), emotional learning and memory (fear conditioning), nociception and motor ability. For select assays in which *Pten* haploinsufficient mice

display abnormalities, we are testing drugs that modulate the serotonin pathway as candidate suppressors.

Results: Results from our battery suggest that *Pten* haploinsufficient males display greater immobility in the tail suspension test, indicating a higher level of depression-like behaviour. We also find that *Pten* haploinsufficient show abnormalities in assays of dark-light emergence and fear conditioning.

Conclusions: These data indicate that haploinsufficiency for *Pten* results in abnormalities in mood and anxiety, as well as emotional learning and memory, with implications for understanding comorbidities in individuals with ASD. Ongoing experiments are investigating potential developmental mechanisms.

105.008 8 Chronic Neuroinflammation and Altered Inflammatory Responses in a Mouse Model of Autism. L. Lucchina, N. Kazlauskas, M. Campolongo and A. M. Depino*, *IFIByNE, UBA-CONICET*

Background: Several reports have associated peripheral and central alterations in the inflammatory and immune responses with autism spectrum disorders (ASD). However, the consequences of these inflammatory processes on the behavioral symptoms of ASD have not been extensively studied.

Objectives: Our aims are (1) to evaluate the extent of neuroinflammation in a mouse model of ASD, and (2) to evaluate whether the inflammatory response is altered in this model.

Methods: We injected pregnant mice with 400 or 600 mg/kg valproic acid (VPA), at gestational day (GD) 12.5. We then evaluated social interaction and anxiety-related behaviors of the offspring. Moreover, we evaluated the inflammatory response to a peripheral LPS challenge. 2 hs after a 25 mg/kg intraperitoneal LPS injection, we measured plasma corticosterone and the expression of cytokines in the spleen and in regions of the brain relevant to ASD (the cerebellum, the cortex and the hippocampus). Furthermore, we evaluated the number of microglial cells and the area occupied by astrocytes in those same areas.

Results: We confirmed that prenatal exposure to VPA at GD12.5 results in reduced social interaction in adulthood, in the F1 hybrid offspring. Moreover, VPA exposure results in increased anxiety-related behavior. VPA-exposed mice show an exacerbated inflammatory response in adulthood. 2 hs after the LPS injection, plasma corticosterone levels are higher in VPA mice than in controls. Moreover, LPS induces the expression of IL-1 β , IL-6 and TNF- α in the spleen, but the increase of IL-6 is significantly higher in animals prenatally exposed to VPA. When we evaluated the central inflammatory response to a peripheral stimulus, we also found evidence of an exacerbated response. IL-1 β and IL-6 are specifically induced in the cortex of VPA-exposed animals challenged with LPS, and not in control animals. Moreover, although LPS induced the expression of IL-6 and TNF- α in all groups, this increment was significantly higher in animals prenatally exposed to VPA. Finally, animals prenatally exposed to 600 mg/kg VPA have more microglial cells in the hilus of the dentate gyrus and in the CA1 of the hippocampus. Animals prenatally exposed to 600 mg/kg VPA have more microglial cells in the cerebellum, but they show no differences in the number of these cells after a peripheral inflammatory challenge.

Conclusions: Our results further validate the VPA mouse model of ASD, showing that the reduction of social interaction is independent of the genetic background of the animals. On the contrary, the effect of VPA on anxiety-related behaviors appears to be modulated by genetic factors. We found that animals exposed to VPA show an exacerbated response to an inflammatory stimulus, evidenced as increased activation of the hypothalamus-pituitary-adrenal axis, and increased expression of pro-inflammatory cytokines in the periphery and in certain, specific regions of the brain. In addition, we found evidence of neuroinflammation in the cerebellum of VPA-exposed animals. These results show that the VPA model of ASD also models the neuroinflammation and the alterations in the inflammatory response previously documented in ASD patients.

105.009 9 Disruption of the RNA-Binding Protein Celf6 in Mice Results in the Expression of Autistic-Like Behaviors. M. A. Rieger*, S. E. Maloney, D. F. Wozniak, N. G. Mahieu, G. J. Patti and J. Dougherty, *Washington University*

Background:

The complexity of the nervous system presents a challenge to elucidation of molecular and cellular mechanisms underlying psychiatric conditions such as autism spectrum disorders. Innovative methods that can reduce this complexity by focusing on relevant systems may help elevate signal above noise. Dysregulation of the serotonergic system has long been implicated in autism. By specific profiling of serotonergic neurons using the Translating Ribosome Affinity Purification (TRAP) methodology, we uncovered a number of enriched transcripts in these cells, including the RNA-binding protein Celf6, of unknown function in the CNS. A rare variant introducing a premature stop codon in human *CELF6* was found to be significantly associated with autism in human datasets. We hypothesized that disruption of Celf6 in mice would result in perturbation of some autism-related behaviors.

Objectives:

To assess the contribution of Celf6 to the etiology of autism by analysis of relevant behaviors in a murine model.

Methods:

Celf6^{-/-} (n=23) and WT (n=23) C57Bl6/j mouse pups were tested for ultrasonic vocalization induced by maternal separation. Emitted vocalization was measured from the audio recordings, as well as temporal and spectral characteristics of the emitted calls, using automated computational analyses. A separate cohort of Celf6^{-/-} (n=11) and WT (n= 9) adult mice was tested for exploratory behavior in the holeboard maze as well as sociability in the three-chambered social approach assay. Mice of both genotypes were also tested for levels of neurotransmitters by mass spectrometry of brain tissue.

Results:

Celf6^{-/-} mouse pups showed a 60% reduction in the amount of elicited ultrasonic vocalization (p=0.001), measured by the number of emitted calls. Celf6^{-/-} mouse pups did not differ significantly in body weight or temperature,

suggesting differences were not due to gross developmental delays nor environmental conditions at the time of testing. We found no significant change to Celf6^{-/-} temporal characteristics (call duration and inter-call intervals) nor spectral complexity (as measured by percentage of frequency jumps), suggesting that the deficit was not one of physical production. Furthermore, although there was no significant difference in sociability between genotypes, WT adults significantly increased exploratory activity following familiarization with a food reward (p=0.002) compared to Celf6^{-/-} mice. Finally, we found that Celf6^{-/-} mice had a significant ~20% reduction to brain serotonin levels (p<0.002) but not other neurotransmitters such as GABA or glycine.

Conclusions:

Our findings suggest Celf6^{-/-} pups do not respond as readily as WT animals to a social cue and this is not due to physical inabilities. Furthermore, Celf6^{-/-} mice do not appear to modify behavior as adults in response to reward. These data point to both communication deficits and resistance to change in the Celf6^{-/-} model. Future investigations will probe the molecular role of Celf6 in the the development and maintenance of the serotonergic system, adding to the body of knowledge on the cellular mechanisms underlying these complex behaviors. Our results show that expression profiling of specific cell populations facilitates screening for genes contributing to relevant phenotypes in psychiatric disorder, and they identify Celf6 as a gene contributing to the expression of some autistic-like behaviors.

105.010 10 FOXP2 in the Nucleus Accumbens Regulates Reward Signaling and Social Behavior. C. Mombereau^{*1}, V. Medvedeva¹, T. Ghosh¹, D. Herve¹, C. French², S. E. Fisher³, W. Enard⁴, S. Pääbo⁴, E. Ben David⁵, S. Shifman⁵, M. Mameli¹ and M. Groszer¹, (1)*Institut du Fer a Moulin*, (2)*Champalimaud Neuroscience Programme*, (3)*Max Planck Institute for Psycholinguistics*, (4)*Max Planck Institute for Evolutionary Anthropology*, (5)*The Hebrew University of Jerusalem*

Background: Disturbances of speech and language are part of a large variety of neuropsychiatric syndromes including autisms. The complex genetic architecture of these disorders and their speech and language related

endophenotypes cause substantial problems in the identification of underlying molecular and neuronal networks. Previously a human mutation in the forkhead-box transcription factor *Foxp2* has been identified as the first example of a gene specifically implicated in a speech and language disorder. While the speech endophenotypes have been very instrumental in initial genetic mapping, it has long been suggested that critical roles of *FOXP2* might lie further 'upstream' than the motor system. *Foxp2* is highly conserved in genomic structure and neuronal expression pattern and thought to play important roles in development and/or function of cortical and striatal neuronal circuits. Our previous studies in *Foxp2*^{+/-} mice suggested a close interaction between this transcription factor and the dopaminergic system with potentially important implications for reward associated behavior.

Objectives: We aimed to study the potential role of *Foxp2* in DA signaling, to identify involved neuronal circuits and to dissect developmental from adult functions of *Foxp2* in reward associated behavior and social interaction. Finally we explored DA activity dependent *Foxp2* transcriptional targets in reward circuits.

Methods: We used robust neuropharmacological approaches, extensive behavioral analysis, electrophysiology and genomic approaches in *Foxp2*^{+/-} and *Foxp2* conditional mutant mice.

Results: *Foxp2*^{+/-} mice exhibit a severely attenuated cocaine-induced hyperlocomotion response and significantly decreased ERK phosphorylation elicited by cocaine compare to *Foxp2*^{+/+}. The ERK signaling deficit was specifically detected in the nucleus accumbens (Nac) but not in the dorsal striatum. *Foxp2* mRNA and protein level were acutely (1h) downregulated in the NAc but not the dorsal striatum 1h following cocaine. DA signaling in the NAc is particularly implicated in associative reward-relating learning and social behaviors, we employed conditioned place preference (CPP) to cocaine and social interactions paradigms in *Foxp2* deficient mice. We observed that CPP and social behaviors are impaired in *Foxp2*^{+/-} mice. NAc-specific deletion in adult *Foxp2*^{lox/lox} mice recapitulated the impaired cocaine-induced hyperlocomotion response and social interaction deficits found in

Foxp2^{+/-} mice. These alterations were associated with deficits in high frequency stimulation induced LTP at cortico-striatal synapses from cortical projections to the NAc, a key synaptic plasticity mechanism for reward learning. Finally, Nac transcriptome profiling in *Foxp2* deficient mice following DA stimulation, identify gene networks underlying the role of *Foxp2* on reward processing.

Conclusions: Our data suggest that *Foxp2* in Dopamine 1 receptor expressing medium spiny neurons (MSNs) in the Nac has neuronal activity-dependent functions in DA mediated reward signaling. These results resonate with clinical and imaging studies in autism spectrum disorders (ASD) suggesting that social motivation deficits due to decreased reward value for social stimuli as a key pathomechanism. The decreased salience of social stimuli such as faces is thought to profoundly impair the later development of social cognition and language. In this context our results suggest that exploring *Foxp2* regulated gene networks in nucleus accumbens MSNs might provide new insights into conserved molecular and cellular mechanisms of social decision making (SDM) networks.

105.011 11 Generation of a Transgenic Mouse Model to Inhibit the Function of Beta-Neurexin-1, a Gene Involved in Autism Spectrum Disorders. L. Garcia Rabaneda^{*1}, E. Robles-Lanuza¹, M. L. Pecero¹, J. A. Paez-Gómez¹, A. Martinez-Mir² and F. G. Scholl¹, (1) *Instituto de Biomedicina de Sevilla, Hospital Universitario Virgen del Rocío/CSIC/Universidad de Sevilla. Departamento de Fisiología Médica y Biofísica*, (2) *Instituto de Biomedicina de Sevilla, Hospital Universitario Virgen del Rocío/CSIC/Universidad de Sevilla*.

Background:

Synapses are established with precision during brain development and are constantly remodeled as a consequence of synaptic activity in the adult networks. Synaptic dysfunction underlies the molecular basis of several neurodevelopmental disorders, such as autism spectrum disorders (ASD). Trans-synaptic adhesion systems can regulate synaptic function, as they organize pre- and postsynaptic protein complexes. One of these adhesion systems is formed by neurexins and neuroligins. These proteins promote the assembly and maturation of synapses through a

bidirectional mechanism. In mammals, neuroligins are encoded by three genes with two alternative promoters, which produce the long (alpha-neuroligins) and the short (beta-neuroligins) isoforms. In addition, alternative splicing in the extracellular domain contributes to generate hundreds of neuroligins isoforms. Despite the high heterogeneity of the extracellular region, the cytoplasmic domain is common to all neuroligin isoforms and it is thought to regulate intracellular signalling. The relevance of neuroligins in neurodevelopmental disorders has been highlighted by the identification of mutations in neuroligin genes in ASD. Recently, we have suggested a role for synaptic defects of beta-neuroligin-1 as a risk factor for autism and mental retardation.

Objectives:

To characterize in cultured neurons the effect of a beta-neuroligin-1 dominant negative mutant that lacks the cytoplasmic tail (HA-bNrx1DC). To inhibit the function of beta-neuroligin-1 *in vivo* by expressing the HA-bNrx1DC mutant. To characterize the behavioral phenotype of a double transgenic mice expressing an inducible form of the HA-bNrx1DC mutant (TRE-HA-bNrx1DC/CamKII-tTA).

Methods:

In vitro studies have been performed in hippocampal neurons at 10-14 DIV isolated from 18-19 embryonic day rat brains. For *in vivo* studies we have generated a transgenic mouse line that expresses a HA-tagged beta-neuroligin-1 mutant lacking the cytoplasmic domain (HA-bNrx1DC) under the control of the inducible TRE promoter. The TRE-HA-bNrx1DC transgenic mice have been crossed with CAMKII -tTA animals to direct the expression of the mutant protein to glutamatergic terminals *in vivo*.

Results:

Our *in vitro* results suggest that HA-bNrx1DC mutant can function as a dominant negative mutant as it can be recruited to the membrane of glutamatergic synapses through interaction with neuroligin-1, but it inhibits intracellular signalling mediated by the cytoplasmic tail. *In vivo* we show

expression of HA-bNrx1DC in the cortex and hippocampal formation by immunolocalization. Moreover, we have evaluated the behavioral consequences of the lack of beta-neuroligin-1 function in TRE-HA-bNrx1DC/CamKII-tTA double transgenic mice.

Conclusions:

Inducible expression of a beta-neuroligin-1 dominant negative mutant might have implications in the study of autism, as it may help answering to what extent synaptic and behavioral defects due to beta-neuroligin-1 dysfunction can be rescued by resuming normal beta-neuroligin-1 function.

105.012 12 Social and Vocal Behaviors of a Novel ASD Mouse Model. J. M. Bowers* and G. Konopka, *UT Southwestern Medical Center*

Background: Autism, or the more broadly defined autism spectrum disorders (ASDs), is multifaceted and likely due to a combination of genetic and environmental interactions. Two of the core deficits in ASD are abnormal social interactions and impairments in the ability to use language. Several genetically engineered mice have been developed in order to experimentally address these behavioral characteristics. Because disrupted communication is a core feature of ASD and language is a human-specific feature, it is particularly challenging to study this aspect in non-human animal models. Previous studies have uncovered ASD patients with mutations in *FOXP1*. *FOXP1* is a transcription factor and a member of the *FOXP* family of genes. A closely related family member, *FOXP2* has been linked to language impairment in humans and alterations in ultrasonic vocalizations in mice.

Objectives: Due to the direct association of *FOXP2* to language and vocalization and its close association to *FOXP1*, we explored the potential connection of *FOXP1* to vocalizations. Thus, we ascertained whether mutation of *Foxp1* in rodents would have an impact on social and vocal behaviors.

Methods: We conducted a wide array of behavioral tests including open field, social preference, and ultrasonic vocalizations among others.

Results: We observed a distinctive difference in the ability of the *Foxp1* mutant mice to perform at comparable levels to wild-type litter mates on assays testing social interaction and learning. In addition, analysis of pup vocalizations revealed distinct differences in the developmental pattern of the *Foxp1* mutant mice versus wild-type litter mates.

Conclusions: A preliminary interpretation of these differences suggests the vocalization repertoire of the *Foxp1* mutants is delayed. This delay in the production of maternal separation calls might be an early indicator of abnormal social behaviors and learning impairments caused by altered levels of Foxp1. Together, these data suggest that *Foxp1* mutant mice may be a novel model system for the study of ASD pathophysiology.

105.013 13 Gestational Exposure to Anticonvulsant Valproic Acid (VPA) Stimulates Forebrain Neurogenesis and Leads to Postnatal Brain Enlargement. X. Zhou* and E. DiCicco-Bloom, *Robert Wood Johnson Medical School*

Background: Exposure of the developing embryo to VPA is known to induce developmental defects in central nervous system, including signs of autism spectrum disorder (ASD). Mechanistic studies in developmental models have identified many signaling pathways including AP-1 transcription factor, P-ERK, GSK3b, ion channels, HDAC and epigenetic changes. Although recent studies of chronic drug exposure in adult brain models of depression and neurogenesis suggest VPA stimulates mitogenesis via P-ERK and HDAC, earlier studies in neural crest, neuroblastoma and glial cell lines indicate VPA inhibits proliferation and promotes cell differentiation. We now define effects of VPA on embryonic rat cerebral cortical precursors both in culture and in developing animals.

Objectives: To define the developmental effects of VPA on forebrain neurogenesis through in vitro and in vivo experiments.

Methods: In vitro, embryonic day 14.5(E14.5) cerebral cortex precursors were cultured without or with VPA. In vivo, pregnant moms at E16.5 received 2 doses of VPA/day at 300mg/kg body weight for a total of 1~5 doses. DNA synthesis was analyzed using incorporation of cell cycle markers [³H]-thymidine and BrdU; VPA effects on

neurite outgrowth were analyzed using phase microscopy of live cells. Second messenger and cell cycle mechanisms were assayed using Western blotting. The differentiated cell populations of the brain were assessed at postnatal day 21 (P21) through unbiased stereology and immunohistochemistry for cell type-specific markers. Brains were weighed at P21, with 35 rats for the control and 33 rats for VPA exposed groups.

Results: VPA had similar effects on DNA synthesis of cortical precursors both in culture and in developing brain, increasing [³H]-thymidine incorporation by 25% and 23%, and BrdU labeling index by 20% and 53.7%, respectively, compared to control (N=10-15/group; p<0.01). These observations indicate that VPA increased the entry of cells into mitotic S phase. In addition, VPA increased the percent of cells expressing precursor marker nestin by 68.8% while decreasing process-bearing cells by ~50%, suggesting VPA inhibited the transition from proliferation to differentiation. At the level of mechanism, VPA stimulated cell cycle regulators, increasing levels of both cyclin-D3 and E proteins as early as 1h after exposure, suggesting that VPA rapidly alters cell cycle mechanisms to enhance neurogenesis. Further, to define mediating pathways we assessed second messengers and found VPA increased levels of acetylated histone H3, but not levels of activated ERK, AKT, GSK3 or PKC. Finally, the stimulatory effects of VPA in vitro were directly relevant to brain development in vivo: VPA exposure during gestation increased brain weight measured at P21 by 4% and total cell number by 13.8%. The increase in total cell number consisted primarily of neurons, as indicated by pan neuronal marker, NeuN, and neuronal layer-specific markers, Cux1 and Tbr1, which were increased by 14.3%, 26.4%, and 15.4%, respectively.

Conclusions: Embryonic exposure to VPA maintains forebrain precursors in the cell cycle and reduces neuronal differentiation. VPA likely acts via inhibiting histone de-acetylation and increasing cyclin-D3 and E to promote forebrain neurogenesis. These developmental effects of VPA may be relevant to brain enlargement observed in some cases of ASD.

105.014 14 Immune Deficiency Affects Juvenile Social Behavior in Mice and Is Altered by Splenocyte

Transfer. K. M. Quinnes*¹, K. H. Cox¹ and E. Rissman², (1)University of Virginia, (2)University of Virginia School of Medicine

Background: Severe Combined Immunodeficiency (SCID) mice are frequently used for immunological research, however, little behavioral work has been conducted using these mice. Although SCIDs grow and develop normally, adults display impaired learning in comparison to wild type C57BL/6 mice, which can be rescued with splenocyte transfer, and more specifically T cell replacement. It has been hypothesized that immune deficiency is linked to autism spectrum disorders.

Objectives: To test whether juvenile social behaviors are altered in mice with severe immune deficiency and determine whether an injection of healthy splenocytes modifies behavioral differences.

Methods: Male SCID and wild-type (WT) C57BL/6J mice were tested for social and anxiety behaviors between postnatal days 21 and 27 (after weaning but before puberty onset) in an elevated plus maze, social preference task, and social recognition task. A second group of mice received splenocyte transfers from an age matched C57BL/6J mouse, and behavior was evaluated in these groups as well.

Results: Young SCID mice spent more time investigating a novel mouse than did C57BL/6J juveniles, displayed impaired responses to unfamiliar mice in the social recognition task and were more anxious than controls in the elevated plus maze. A second set of SCID mice received saline or donor splenocytes on post-natal day 7. When tested in the same tasks, splenocyte transfer changed behavior in the social recognition task, and the social preference task. In the social recognition task, behavior was rescued to that of a C57BL/6J mouse with an intraperitoneal injection of healthy splenocytes on P7. Following the injection SCID mice that received splenocytes had a reduced preference in the social novelty task compared to C57BL/6J mice and SCID mice that did not receive splenocytes.

Conclusions: These data reveal that the immune system is important for juvenile social behavior related to autism spectrum disorders and that

splenocyte transfer can mitigate some of these social deficits.

105.015 15 Population-Based Prevalence of Autism Spectrum Disorders (ASD) in a Hispanic Population: Puerto Rico, 2011. J. F. Cordero*, A. F. Alonso, H. F. Mattei and I. Torres, *UPR School of Public Health*

Background: Although it is now recognized that Autism spectrum disorders (ASD) is highly prevalent, there is limited data on the epidemiology of ASD in Hispanic populations. We conducted a population-based survey of ASD among 4 to 17 year old children in Puerto Rico (PR) in 2011.

Objectives: Estimate the prevalence of ASD in PR, its comorbidities, and the impact on the health system.

Methods: Conducted a telephone-based random-digit-dial of the 9 health regions of PR using a structured survey based on questions of the National Survey of Children Health (NSCH) and the National Health Interview Survey (NHIS) translated to Spanish. ASD was defined based on parent or guardian report: a health care provider indicated that the child has an ASD.

Results: The prevalence of ASD was 1.62% [95% IC: 1.4-1.9]. The male:female ratio was 6.5:1. Prevalence by health region was similar and not statistically different from the island-wide rate of ASD. Comorbid disorders were prevalent (92%) including epilepsy (10%), gastrointestinal conditions (30%), food allergies (23%) and respiratory allergies (30%) among others. Insurance coverage was 98%, but nearly half reported that insurance did not cover the needed health services needed. **Conclusions:** ASD in Puerto Rico among the highest in the United States following New Jersey and Utah. Comorbid conditions are common among individuals with ASD and there is an important gap in coverage of needed health services among insured. These results underscore the urgent need to increase efforts enhance and address needs of families impacted by ASD at all ages in Puerto Rico and beyond.

105.016 16 Implication of Engrailed 2, an Autism Associated Gene, in Hippocampal Neurogenesis, Apoptosis and Synaptic Activity. M. Genestine*¹, M. T. Durens¹, S. Hu¹, M. Plummer², Z. Pang³, J. H. Millonig⁴ and E.

DiCicco-Bloom¹, (1)Robert Wood Johnson Medical School, (2)Rutgers University, (3)Child Health Institute of New Jersey, (4)CABM

Background:

Autism etiology includes both environmental and genetic risk factors. One genetic factor is the *Engrailed 2 (En2)* gene, which we found associated with Autism Spectrum Disorder in 3 different datasets, and disease associations have been reported by 6 other groups. *En2* is a transcription factor that is expressed in and patterns mid/hindbrain and cerebellar structures, acting both pre- and post-natally.

Surprisingly, in previous work, we found *En2*-knock out (*En2*-KO) mice exhibited deficits in the forebrain, a region outside its classical hindbrain localization. In the hippocampus, norepinephrine (NE) levels were reduced by 33%, and there were reductions in hippocampal weight (-12%), DNA content (-16%) and dentate gyrus neurons (-16%). The decrease in hippocampal neurons was associated with a 77% increase in cell death (caspase3+, pyknotic body), and while progenitor cell proliferation (BrdU+, PCNA+) was increased 2-fold, newly born (BrdU+) cells at P21 underwent excessive cell death, suggesting dysregulation of neurogenesis. These data led to the hypothesis that deficits in NE in the *En2*-KO may result in enhanced programmed cell death, and that neurogenesis may increase in compensatory fashion.

Behavioral studies in the *En2*-KO indicate deficits in social interaction and hippocampal-dependent behaviors. Significantly, both post-natal neurogenesis and synaptic plasticity are critical for learning and memory. We now explore the nature of progenitors cell death and define long term potentiation (LTP), a form of synaptic plasticity, in the *En2*-KO.

Objectives:

By defining the deficits caused by *En2* mutation, we aim to identify new biological functions downstream of *En2*. We are using the hippocampus as a model structure to understand *En2*'s influence on neurogenesis and synapse function hoping to generalize finding to other brain regions and reveal new treatment avenues.

Methods:

Immunohistochemical markers of neural progenitor cells (Sox2, Dcx) and proliferation (BrdU) were assessed. Field Excitatory Post-Synaptic Potential (fEPSP) recordings were performed on 1 month old hippocampus slices, stimulating the Schaffer collateral pathway while recording in the CA1 stratum-radiatum. We measured synaptic transmission, paired pulse facilitation and LTP.

Results:

The *En2*-KO dentate gyrus exhibited increased proliferation at P21 that reflected early neural progenitors (Sox2+) only (N=5/genotype; $p < 0.02$). They were increased in cell number (+17%) as well as proliferative activity (+219%). In contrast, there were no changes in later progenitors (Dcx+).

In *En2*-KO hippocampal slices, fEPSPs were normal, including synaptic transmission and paired pulse facilitation (N=10/genotype). In contrast, preliminary data suggest increased LTP in *En2*-KO (+17%) compared to WT (+8%). Based on enhanced LTP, we are now examining the GABA-inhibitory neuron population, which may be decreased. Preliminary data show decreased in Parvalbumine-population interneurons (-17%).

Conclusions:

These studies suggest that in the absence of hindbrain patterning gene *En2*, there are many consequences for hippocampal neuron production, survival and function. While currently speculation, changes in forebrain neurogenesis and synaptic plasticity may be due to diminished NE, which affects both processes. Further, recent behavioral studies show that a NE re-uptake inhibitor can reverse *En2*-KO deficits in both social and hippocampal-dependent tasks. Potentially, altering monoamine levels during development may correct forebrain structural deficits and improve functional abnormalities.

105.017 17 Incidence of Impaired Social Behavior As Reported by Owners and Breeders of Miniature and Standard Poodles. R. M. Zamzow^{*1}, K. L. Jones², E. C.

Reznicek², L. Lit³ and D. Q. Beversdorf², (1)*University of Missouri-Columbia*, (2)*University of Missouri*, (3)*University of California-Davis*

Background: Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by social interaction deficits, communication impairments, and restricted, repetitive behaviors. Human clinical samples of ASD are limited by genetic heterogeneity in the investigation of this disorder's genetic underpinnings. Individual dog breeds offer genetic homogeneity, allowing for a targeted investigation of genetic components of complex behavioral traits, such as social interaction. Previous work has proposed multiple examples of alterations in genes that result in similar disorders for both humans and dogs, validating the utility of using the dog as a model for human traits.

Objectives: The present study examines social interaction in miniature and standard poodles, breeds previously described as being less social overall than other breeds, using an owner-report survey with questions adapted from the human Autism Diagnostic Observation Schedule (ADOS). The primary aim of this study was to determine the existence of subgroups within each breed that demonstrate significantly less social behavior than other dogs within the breeds. We also sought to confirm factor loadings determined by a previous study utilizing the owner-report survey and to compare identified subgroups in terms of these factors.

Methods: Survey questions adapted from the ADOS to pertain to dog social interaction behavior were included as part of an online survey used to collect data. Questions were structured as likert-type scales, ranging from 0 to 2 to 0 to 4, depending on the question. Data analyzed was restricted to fully completed surveys for AKC or CKC-registered miniature and standard poodles.

Results: Cluster analyses using standardized data were utilized to determine the existence of a subgroup of dogs within each breed that demonstrates significantly reduced social behavior as compared to other dogs within the breeds. For both breeds a k-means cluster analysis for two clusters identified one small and one large cluster differing significantly in social behavior. In both breeds, the smaller clusters represent subgroups

of dogs with lower scores on the social interaction questions. A previous study identified three factors examined by the survey: initiation of reciprocal social behaviors, response to social interaction, and communication. Although the sample sizes in each breed for the present study prohibited confirmatory factor analyses, experimental factor analyses revealed similar loadings for individual questions onto each of the three factors. One-way ANOVAs or Welch's variance-weighted ANOVAs were used to compare the identified clusters in terms of factor scale scores. The less social subgroup of both miniature and standard poodles demonstrated significantly decreased scale scores across all three factors, as compared to the more typical subgroups. Thus, for both breeds, the dogs identified as having reduced social behavior differed from the remainder of the dogs on all the three social domains assessed by the survey questions.

Conclusions: The identification of these subgroups demonstrating reduced abilities across several domains of social interaction suggests a potential genetic component in social behavior that could be further examined in both dogs and humans.

Future investigation will involve behavioral observation and genetic analysis for potential mutations underlying atypical social behavior in miniature and standard poodles.

105.018 18 Letting a Typical Mouse Judge Whether Mouse Social Interactions Are Atypical. C. R. Shah*¹ and J. Veenstra-VanderWeele², (1)*Vanderbilt University*, (2)*Monroe Carell Children's Hospital at Vanderbilt University*

Background: Diagnosis of an autism spectrum disorder (ASD) requires a qualitative assessment of social aptitude: one person judging whether another person interacts in a 'typical' way. Thus far, quantitative assessment of behavior has not been used in diagnosis of autism. In contrast, genetic or behavioral mouse models of autism are typically evaluated by quantification of social behavior, either by time spent in proximity to another mouse or by particular behaviors exhibited during direct social interactions.

Objectives: Rather than quantifying mouse behavior during social interactions, we hypothesized that a typical mouse could be used to make a judgment of another mouse's social behavior. We used a three-chamber paradigm to

ask whether typical mouse 'judges' prefer 'typical' over 'atypical' social interactions with mouse models relevant to ASD.

Methods: We used wildtype C57BL/6 (B6) mice as 'judges' and evaluated their preference for a chamber containing a 'typical' (B6 or 129S6) or an 'atypical' mouse. For our atypical mouse stimuli, we chose two inbred strains with well-documented social phenotypes (BTBR and BALB/c), as well a mutant line with abnormal social behavior and seizures (*Gabrb3* +/-).

Results: Overall, we observed a stimulus by time interaction ($P < 0.0001$), with B6 mice preferring the typical mouse chamber during the last 10 minutes of the 30-minute test. For two of the individual stimulus pairings, we observed a similar chamber by time interaction (BALB/c vs. 129S6, $P = 0.0007$; *Gabrb3* +/- vs. 129S6, $P = 0.033$). For the third stimulus pairing, we found a trend for preference of the typical mouse across time (BTBR vs. B6, $P = 0.051$). We repeated the experiments using 129S6 mice as judges and found a significant overall interaction ($P = 0.034$), but only one stimulus pairing reached significance on its own (BALB/c vs. 129S6, $P = 0.0021$).

Conclusions: These data suggest that a characteristic pattern of exploration in B6 mice can distinguish some socially atypical animals from controls. These data need to be replicated across laboratories to evaluate whether mouse preference for typical social interactions may be useful to evaluate social competence in mouse models relevant to autism spectrum disorders.

105.019 19 Loss of Dvl1 and 3 Induces Early Brain

Overgrowth Via Transcriptional Deregulation of Beta-Catenin, Brn2 and Tbr2. H. Belinson^{*1}, J. Nakatani¹, R. Y. Birnbaum¹, N. Ahituv¹, R. J. McEvilly², M. G. Rosenfeld² and A. Wynshaw-Boris¹, (1)*Institute for Human Genetics, UCSF*, (2)*San Diego School of Medicine, UCSD*

Background: The development and growth of the brain is regulated by the highly conserved wingless/Wnt signaling pathway. The Dishevelled (Dvl) family of proteins, consisting of Dvl1, Dvl2 and Dvl3 relay Wnt signals from receptors to downstream effectors. Wnt canonical downstream effector, β -Catenin, is a regulator of gene expression and cell fate specification. Previous studies of adult *Dvl1*-null mice revealed abnormal

social interactions, without any gross pathological brain abnormalities.

Objectives: We set out to test the hypothesis that additional reduction of Dvl allele may display pathological brain abnormalities during development.

Methods: *Dvl1*^{-/-3+/-} mice were generated and analyzed for early brain overgrowth, an established autistic phenotype.

Results: We found that *Dvl1*^{-/-3+/-} mice display early embryonic brain overgrowth associated with induced proliferation and early expansion of cortical basal neural progenitors *in vivo* and *in vitro*. Induction of brain overgrowth was regulated by a cascade of transcriptional activity. β -catenin transcriptional activity was reduced in the *Dvl1*^{-/-3+/-} neural progenitors which resulted in down-regulation of Brn2. Using Chromatin Immunoprecipitation (ChIP), we showed that Brn2 directly binds to and inhibits the expression of the basal transcription factor Tbr2. Thus in *Dvl1*^{-/-3+/-} mice reduced Brn2 expression gave rise to Tbr2 upregulation, which consequently induced proliferation of the basal progenitor cells and their neuronal progeny in the cerebral cortex. Dvl mutant phenotype could be rescued using both genetic and pharmacological manipulations of Dvl downstream effectors.

Conclusions: Thus, we suggest that early brain overgrowth seen in *Dvl1*^{-/-3+/-} mice is mediated by deregulation of the β -catenin/Brn2/Tbr2 transcriptional cascade, which may contribute to the social behavioral phenotype in the adult *Dvl1*^{-/-3+/-} mice.

105.020 20 Modulation of RhoGTPases by the Bacterial Protein CNF1 Improves the Neurobehavioural Phenotype in a Mouse Model of Rett Syndrome. B. De Filippis^{*}, A. Fabbri, R. Canese, L. Ricceri, F. Malchiodi-Albedi, C. Fiorentini and G. Laviola, *Istituto Superiore di Sanità*

Background: RhoGTPases are crucial molecules in neuronal plasticity and cognition, as confirmed by their role in non-syndromic mental retardation. Activation of brain RhoGTPases by the bacterial Cytotoxic Necrotizing Factor 1 (CNF1) reshapes the actin cytoskeleton and enhances neurotransmission and synaptic plasticity in mouse brains. Recently, Rho GTPases signaling

pathways have been suggested to be involved in the pathophysiology of a clinical variant of Rett syndrome (RTT). Classified together with autism into the DSM-IV in the group of pervasive developmental disorders, RTT is a rare neurodevelopmental disorder primarily affecting girls with a prevalence of 1:10,000 births, for which no effective therapy is available.

Objectives: We evaluated whether pharmacological interventions targeting RhoGTPases may be an effective therapeutic strategy for RTT. **Methods:** To this aim, we performed a single CNF1 intracerebroventricular (icv) inoculation in a RTT mouse model, which expresses a truncated form of the MeCP2 gene (MeCP2-308 mice). Fully symptomatic MeCP2-308 male mice were subsequently evaluated in a battery of tests specifically tailored to detect RTT-related impairments. At the end of behavioral testing, brain sections were immunohistochemically characterized. Magnetic resonance imaging (MRI) and spectroscopy (MRS) were also applied to assess morphological and metabolic brain changes. **Results:** The CNF1 administration markedly improved the behavioral phenotype of MeCP2-308 mice. CNF1 also dramatically reversed the evident signs of atrophy in astrocytes of mutant mice and restored wt-like levels of this cell population. CNF1-induced brain metabolic changes detected by MRS analysis involved markers of glial integrity and bioenergetics, and point to improved mitochondria functionality in CNF1-treated mice. **Conclusions:** These results clearly indicate that modulation of brain RhoGTPases by CNF1 may constitute a totally innovative therapeutic approach for RTT and, possibly, for other neurodevelopmental disorders.

105.021 21 Mouse Models of Autism Phenotypes As Preclinical Screening Platforms for Novel Oxytocinergic Compounds. B. L. Teng*¹, R. J. Nonneman¹, V. D. Nikolova¹, K. L. Agster¹, T. T. Davis², N. V. Riddick¹, L. K. Baker¹, C. A. Pedersen¹, M. B. Jarstfer² and S. S. Moy¹, (1)University of North Carolina School of Medicine, (2)University of North Carolina

Background: There is emerging evidence that oxytocin (OT) treatment can improve social deficits and repetitive behavior in autism spectrum disorders (ASDs). However, administration of the neuropeptide, which has a short plasma half-life and poor ability to penetrate the blood-brain barrier, is a problematic issue for

clinical use. We have recently initiated a drug development program to identify novel, highly selective, non-peptide OT receptor (OTR) agonists. These efforts would be accelerated by animal models to screen drug candidates for efficacy against ASD-relevant phenotypes.

Objectives: Validate mouse models for preclinical screening of compounds that target the OT pathway, in order to facilitate the development of therapeutics for core ASD symptoms.

Methods: BALB/cByJ and C58/J are well-characterized inbred mouse strains that exhibit behavioral phenotypes relevant to ASD. To validate these models as preclinical screens, mice were tested for OT effects on sociability in a three-chamber task and perseverative responses in a marble-burying assay. C58/J was also examined for OT effects on repetitive behavior and open field activity. These screening platforms were then used to evaluate Compound 39 (a synthetic, non-peptide OTR agonist).

Results: The acute OT regimen did not increase sociability in BALB/cByJ. However, the sub-chronic OT regimen (i.e. four intraperitoneal injections across 7-8 days) had significant prosocial effects in both BALB/cByJ and C58/J. Increased sociability was observed 24 hr following the final OT dose in BALB/cByJ, while prosocial effects of OT emerged 1-2 weeks post-treatment in C58/J. An acute OT regimen decreased motor stereotypy in C58/J, at a dose that did not produce sedative or anxiolytic-like effects in open field testing. Similarly, acute OT treatment led to significant reductions in marble-burying by BALB/cByJ. Consistent with previous research, Compound 39 produced some OT-like effects; however, the drug had no effect on sociability.

Conclusions: These studies show that OT reverses social deficits in mouse models of ASD, dependent on dose regimen and genotype. Furthermore, acute OT decreases abnormal repetitive behavior in C58/J and marble-burying in BALB/cByJ. These findings provide validation of the BALB/cByJ and C58/J models as valuable platforms for screening novel drugs for intervention in ASDs, and for elucidating the mechanisms contributing to prosocial and other beneficial effects of OT.

105.022 22 Prenatal Exposure to Group B Streptococcus, Phthalates, and Flame Retardants: A New Animal Model for ASD?. S. Degroote*, J. Bergeron, M. E. Brochu, G. Sébire and L. Takser, *Université de Sherbrooke*

Background: Epidemiological data suggests that: (i) prenatal exposure to phthalates and flame retardants (FRs) can affect mental and motor development, and provoke internalizing behavior; (ii) there is a clear link between ASD and prematurity, frequently associated with chorioamnionitis, for which Group B Streptococcus (GBS) is one of the most frequent causes. We hypothesize that the combination of these two frequent aggressions (GBS and FRs/phthalates) during a critical perinatal period can lead to ASD through a perinatal neuroinflammatory response. In numerous rodent studies, valproic acid, a frequently prescribed antiepileptic drug, has been shown to induce ASD-like behavior including lower exploratory activity, deficit in social behaviors, diminished acoustic prepulse inhibition, delayed nest-seeking response. We therefore used valproic acid as a positive control in our study.

Objectives: To determine the extent to which prenatal exposure to GBS and/or phthalates/FRs induces the full spectrum of autism relevant behavior.

Methods: The study was carried out in 25 pregnant Lewis rats exposed to:

GROUP 1: a mixture of selected FRs and phthalates at low dose (3 phthalate : DEHP, DBP, DiNP; and 2 FRs : BDE-47, BDE-99) (n=7) in peanut oil by gavage from GD15 to delivery;

GROUP 2: inactivated GBS by i.p. injections from GD19 to GD22 and the same mixture of contaminants as in GROUP 1 (n=7) by gavage

GROUP 3: 600mg/kg of valproic acid by i.p. injection at GD12, a positive control group (n=5);

GROUP 4: peanut oil vehicle by gavage from GD15 to delivery (n=6), a negative control group.

The following behavioral tests were administered to offspring: recording of ultrasonic vocalizations (PND7 and PND14), nest-seeking behavior

(PND8), auditory startle (PND11 to PND13), Open Field (PND20), Elevated Plus Maze (PND25), prepulse inhibition (PPI) of the acoustic startle (PND35), and test of social interactions (PND40).

Results: Our preliminary results show that offspring exposed to GBS and contaminants, as well as those exposed to valproic acid, showed significantly more difficulty to find the maternal compartment in nest-seeking behavior and were less active in the Open Field test than control animals. Animals exposed in utero to the mixture of FRs and phthalates were more active in the Open Field and social interactions tests.

In addition, we observed a dramatic effect of valproate acid on gestation in 3 of the 5 dams (non delivery and spots of embryo implantation on the uterus) and on developmental landmarks (decreased birth weight, delayed eye opening and fur growth) in the 2 delivered litters.

Conclusions: Our results suggest that simultaneous prenatal exposure to GBS, phthalates, and FRs induces long term behavioral effects in rat offspring, similar to the features of ASD, including a very attenuated response to maternal presence and substantially less explorative behavior.

105.023 23 Prioritizing Mouse Models for Autism Spectrum Disorder Using A Disease-Specific Phenotype Signature. I. Menashe*, A. Kumar and S. B. Basu, *MindSpec Inc.*

Background: The high genetic and phenotypic heterogeneity of Autism Spectrum Disorders (ASD) poses an enormous challenge for understanding its etiology. Mouse models are excellent tools to study the effect of specific genetic or environmental alterations on ASD-related phenotypes. However, despite the rapid growth in both number and scope of ASD mouse models; there is no consensus about the phenotypic measures (phenoterms) to properly recapitulating this human condition in mice.

Objectives: To address this issue, we investigated phenotypic data from hundreds of ASD mouse models with the goal to prioritize existing ASD mouse models according to their disease-specific phenotype signature.

Methods: Overall, data of 61 commonly used phenoterms belonging to 10 (7 auxiliary and 3 core) phenotype categories from 249 ASD mouse models from AutDB (<http://autism.mindspec.org/autdb/AMHome.do>), and 79 non-ASD mouse models from the Mouse Genome Informatics (MGI) resource (<http://www.informatics.jax.org>) were evaluated. Two-sided Fisher exact test was used to assess the differences in phenotype outcomes between ASD and non-ASD mouse models. Further, a forward stepwise procedure was employed to search for the best combination of phenoterms to separate ASD from non-ASD mouse models. Finally, we used these data to score and rank existing ASD mouse models.

Results: Of the 61 phenoterms, 16 demonstrated significant differences in outcomes between ASD and non-ASD mouse models ($P < 0.05$), and four ('Brain Morphology', $P = 7.5 \times 10^{-10}$; 'Motor Coordination', $P = 1.7 \times 10^{-9}$; 'Locomotor activity', $P = 1.8 \times 10^{-9}$; and 'Cytoarchitecture', $P = 5.3 \times 10^{-8}$) remained significant even after using the conservative Bonferroni correction for multiple testing. Further, a subset of twenty-one phenoterms achieved the best distinction between ASD and non-ASD mouse models (Area Under the Curve [AUC] = 0.82). An alternative algorithm using all 61 phenoterms and assigning high weights to the three core phenotype categories of ASD (Social, Communication, and Repetitive Behaviors), showed a slightly lower classification efficiency (AUC = 0.76). Remarkable variation was seen between model scores reflecting differences in both tested phenotypes and their corresponding outcomes. The highest ranked mouse model by both scoring schemes was the *Pten* conditional knockout, implying a good agreement between core and auxiliary ASD symptoms.

Conclusions: This study provides an initial step towards establishing a standardized battery of phenotypic measures to allow efficient and accurate evaluation of ASD mouse models.

105.024 24 Quantitative Assessment of Social Motivation in Mouse Models Relevant to Autism. L. Martin*, C. Wood, E. Beilstein, H. Sample and M. Gregg, *Azusa Pacific University*

Background: Research on mouse models relevant to autism will benefit from the

development of novel assays of complex social behavior including social motivation. The BTBR inbred mouse strain has previously demonstrated deficits in social behavior among other behaviors that provide some face validity to autism. Comparisons of BTBR mice to the prosocial B6 mice are therefore a reasonable means to validate the assessment of social motivation using novel paradigms. These novel measures can then be used to assess social motivation in mouse models relevant to autism. In recent years, the serotonin and oxytocin systems have been linked to autism. We are therefore exploring the role of these neurotransmitters in social motivation by testing mice lacking the serotonin transporter gene (SERT KO) and mice administered either an oxytocin agonist or antagonist.

Objectives: The goals of this research are to develop and validate new quantitative measures of social motivation in mice and to use these paradigms to assess social motivation in mouse models relevant to autism. Two operant conditioning paradigms that allow a test mouse to control access to another mouse have been developed. Initial research involved testing with BTBR T + tf/J (BTBR) and C57BL/6J (B6) mouse strains for validation purposes. Additional studies are being carried out to determine the role of serotonin and oxytocin systems in social motivation.

Methods: In the social motivation task, test mice are trained to press a lever for a social reward in the form of 15s access to an unfamiliar stimulus mouse. The social reward is set on a progressive ratio schedule with a step size of three. The number of lever presses achieved in the final trial of a testing session (breakpoint) is used as an index of social motivation. In the valence comparison task, motivation for a food reward is compared to a social reward. The mice were conditioned to associate one lever consistently with a food reward and another consistently with the same social reward described in the previous paradigm.

Results: All 9 B6 mice successfully learned to lever press for a social reward, but only 9 of 17 BTBR mice made this learned association. Comparisons between mice that completed testing revealed that BTBR mice had a significantly lower breakpoint than B6 mice ($t=2.741$, $df=16$,

p=.015), indicating lower social motivation in these mice. However, in the valence comparison task, the BTBR mice also obtained significantly fewer food rewards than B6 mice (t=3.321, df=16, p=.004) suggesting that they may have a general deficit in motivation. Testing with the other mouse models is ongoing. In addition to the above novel quantitative measures of social motivation, assessments of social interest and social memory are being conducted through the use of the ANYMAZE video tracking system.

Conclusions: BTBR mice were found to have low levels of social motivation in comparison to B6 controls. However, the BTBR mice also demonstrated significantly fewer lever presses for a food reward in the valence comparison task suggesting low levels of motivation in general.

105.025 25 Reduced Social Interaction, Behavioural Flexibility and BDNF Signalling in the BTBR T+TF/J Strain, a Mouse Model of Autism. M. L. Scattoni, A. Martire, A. Ferrante, G. Cartocci and L. Ricceri*, *Istituto Superiore di Sanità*

Background: The inbred BTBR T+tf/J (BTBR) strain, a putative mouse model of autism, exhibits low levels of social interactions, high repetitive self-grooming levels and unusual pattern of vocalizations when compared to other mouse strains (e.g. the commonly used C57BL/6J strain).

Objectives: In male BTBR and C57BL/6J mice assessment of: i) responsiveness to social and non social cues at adolescence; ii) adult learning and memory of a conditioned fear response; iii) status of BDNF signalling in the hippocampus.

Methods: i) in BTBR and C57BL/6J adolescent mice (30-35-day old) two behavioural tasks involving either social investigation (including evaluation of ultrasonic vocalization rates) in the presence of same strain partner or investigation of inanimate objects; ii) in BTBR and C57BL/6J adult mice fear conditioning test to evaluate learning, memory (and within session extinction) of a fear response; iii) Brain Derived Neurotrophic Factor (BDNF)-induced potentiation in hippocampal slices to evaluate synaptic plasticity, ELISA and western Blot to evaluate protein levels of BDNF and its receptor tyrosine kinase (TrkB) in cortical and hippocampal regions.

Results: BTBR mice showed a reduction of investigation of the social partner, due to a selective reduction of head sniffing, associated with a decrease in ultrasonic vocalizations. No strain differences were detected in object investigation. During fear conditioning, data from contextual retest indicate a BTBR deficit in extinction of the fear response. Subsequent electrophysiological analysis revealed a significant reduction of synaptic transmission in BTBR mice. BDNF and tyrosine kinase B (TrkB) protein levels measured in the hippocampal region were lower in BTBR as compared to C57BL/6J mice.

Conclusions: These data confirm at adolescence the low levels of social interactions in the BTBR strain. At adulthood BTBR mice show a behavioural flexibility deficit (in extinction of the fear response), whereas both biochemical and electrophysiological data point to decreased BDNF signalling (likely due to a reduction in TrkB levels) in the hippocampus of this mouse strain, possibly related to the observed fear extinction deficit.

105.026 26 Social Behavior in Fmr1 Hemizygotic and SAPAP3 Knockout Mice. V. Roman*¹, R. Kedves¹, G. Szabó², F. Erdélyi², Z. Máté² and I. Gyertyán¹, (1)*Gedeon Richter Plc.*, (2)*Institute of Experimental Medicine*

Background: Mounting evidence suggests that a number of psychiatric disorders such as schizophrenia, obsessive-compulsive disorder, intellectual disability and autism spectrum disorder are associated with synaptic defects. Of its myriad of components, the translational repressor FMR1 and the cytoskeletal SAPAP3 proteins are two members of the intricate postsynaptic machinery. While a link between Fmr1 gene mutations and syndromic autism is well established, variations of the Sapap3 gene have been suggested to be associated with obsessive-compulsive disorder and not autism. Yet, a relationship between the SAPAP3 protein and autistic behaviour cannot be ruled out completely. SAPAP proteins belong to the postsynaptic scaffold arching from neurexins to Shank proteins that has also been implicated in autism and dendritic translation of SAPAP proteins is regulated by the FMR1 protein.

Objectives: Earlier studies showed both impaired, unaltered or even higher than normal social behaviour in Fmr1 hemizygotic mice depending on

the background strain, the behavioural assay used and the investigating site. One aim of the present study was to examine whether Fmr1 hemizygotic mice made on an FVB/AntJ background behaved in an asocial way that would support the notion of the use of these mice as a disease model of autism. The other objective of the study was to investigate whether the lack of the SAPAP3 protein resulted in any social behavioural defect.

Methods: Both Fmr1 hemizygotic and SAPAP3 knockout mice were made at the Institute of Experimental Medicine of the Hungarian Academy of Sciences on an FVB.129P2-Pde6b⁺ Tyr^{c-ch}/AntJ and C57Bl/6J background, respectively. In case of Fmr1 mice only males, while in case of SAPAP3 transgenics, both male and female mice were investigated. Social behaviour of the animals was assessed in three assays; the dyadic reciprocal social interaction, the 5-trial social memory and the 3-chamber social preference tests (at ages of 2.5-5 months and 4.5-7.5 months for Fmr1 and SAPAP mice, respectively).

Results: Fmr1 knockout male mice made on an FVB background showed normal social behaviour in all three assays and were not different from their wild type littermates. Both male and female SAPAP3 knockout animals spent more time in active social interaction when compared with the wild type littermates of the same gender. In the 3-chamber sociability assay, both genders showed preference for a gender-matched target mouse. In the 5-trial social memory assay SAPAP knockout mice of both genders produced a typical pattern of habituation and dishabituation however, male knockouts were significantly less active than their wild type littermates.

Conclusions: Social behaviour of Fmr1 knockout mice made on the FVB/AntJ background is not different from their wild type littermates in the assays applied in the present study. SAPAP3 KO mice showed a complex, nevertheless in general normal social behaviour. Notwithstanding the implication of the FMR1 protein in the pathomechanism of autism, the Fmr1 knockout mice on this particular genetic background cannot be used as a disease model of autism. Results of the present study also indicate that SAPAP3 knockouts are not suitable models of defective social behaviour.

105.027 27 Social Communication Deficits in Synapsin II Knockout Mice. C. Michetti^{*1}, M. Morini², B. Greco², F. Benfenati² and M. L. Scattoni¹, (1)*Istituto Superiore di Sanità*, (2)*Istituto Italiano di Tecnologia*

Background:

Autism spectrum disorders (ASD) are heterogeneous neurodevelopmental disorders characterized by deficits in social interaction and social communication, restricted interests and repetitive behaviors. Abnormalities in language development, mental retardation and epilepsy are often observed in autistic children and, conversely, several forms of epilepsy also display ASD. Given the high comorbidity between ASD and epilepsy, the possibility of a common genetic basis for both diseases has been proposed. Synapsins (Syns) are a family of synaptic vesicle phosphoproteins encoded by the *SynI*, *SynII* and *SynIII* genes. The Syn gene family is a good candidate for the synaptic epilepsy/ASD pathway, as Syns regulate synaptic transmission and plasticity with distinct roles in excitatory and inhibitory neurons. Moreover, genetic mapping analysis identified variations in the *SynII* gene as significantly contributing to epilepsy predisposition and a few *SynII* variants potentially associated with epilepsy and ASD. Mice lacking SynII mice experience epileptic seizures starting at 2-3 months of age and display an array of mild cognitive impairments, including emotional and spatial memory deficits. However, the effects of the *SynII* isoform on the various aspects of social behavior have never been studied.

Objectives:

Aim of our study was to analyze whether deletion of *SynII* gene in mice causes social communication deficits at adulthood.

Methods:

Social and vocal repertoires of three month-old Syn II males (n= 11 Syn II^{+/+}, n= 22 Syn II^{+/-}, n= 10 Syn II^{-/-}) were assessed during the male-female interaction test. The 3-min test session was conducted in a clean cage with clean bedding, representing a novel situation for both the male subject and the female partner. Social behaviors and ultrasonic vocalizations were recorded and

subsequently analyzed by Observer X (Noldus) and Avisoft SasLab Pro (Avisoft Bioacoustics).

Results:

Analysis of social and vocal repertoires revealed a clear social investigation deficit (both in frequency: $F(2,40)=3,145$, $P<0.05$ and duration : $F(2,40)=6,343$, $P<0.005$) in *Syn II*^{-/-} male mice associated with an absence of emission of ultrasonic vocalizations ($F(2,40)=3,145$, $P<0.001$) in this social context. Olfactory investigation allows the mouse to gather biologically meaningful information on the identity of a conspecific, such as social status and sex. There is compelling evidence that ultrasonic vocalizations in this context not only serve to establish or to maintain social contact but are predictors of mating opportunities and are associated with reward expectations. Specifically, *Syn II*^{-/-} males showed a significant reduction in nose-to-nose, body and anogenital sniffing toward a sexually receptive female, all behaviors classically performed by mice in this social context. No significant effect of genotype was found on behavioral measurements commonly used to evaluate general exploratory activity

Conclusions:

The social communication deficit observed in *Syn II*^{-/-} mice supports the view that this gene is also involved in the expression of social behavioral traits associated with ASD and suggests as this mutant mouse line represents a good experimental model to study ASD with epilepsy.

105.028 28 Towards Molecular Therapy for Angelman Syndrome. B. J. Bailus*, D. J. Segal and B. Pyles, *University of California Davis*

Background: Angelman Syndrome is a severe form of Autism with the children exhibiting ataxic gait, language and intellectual deficiencies, seizures and sleep disorders. The disease occurs in about 1:12,000 births and is mostly due to de-novo deletions. Angelman Syndrome occurs when an affected individual fails to inherit the normally active maternal *UBE3A*, while the paternal *UBE3A* is silenced, resulting in reduced expression of *UBE3A* in the development of critical brain tissue.

Objectives: In designing an effective gene therapy for Angelman Syndrome, our goal is to reactivate the endogenous, paternal allele of *Ube3a* in an Angelman Syndrome mouse model.

Methods: To accomplish this goal Zinc Finger Artificial Transcription Factors (ATFs) are being utilized. Zinc Fingers are a class of DNA binding proteins that can be programmed to bind to a specific site in DNA. By attaching a repression domains to the Zinc Finger construct an Artificial Transcription Factor is formed, which can suppress transcriptional activity. The therapeutic approach being used involves delivering repressor ATFs to silence *Ube3a-ATS*, a transcript that silences the paternal copy of *Ube3a*. The therapy involves IP injecting purified ATF protein extracts into Angelman Syndrome Mice.

Results: Mice treated with the ATF have shown about a 1.5-1.8 fold increase in whole brain Ube3a protein levels, measured by IHC and Westerns. The ATFs are injected by IP, cross the blood brain barrier; repress the Ube3a-ATS transcript, increasing the expression of the paternal Ube3a.

Conclusions: Inducing paternal Ube3a expression through the use of ATFs can ameliorate the molecular symptoms of Angelman Syndrome. These results should have a broad impact on the Autism Spectrum Field as the same delivery and treatment methodologies can be applied toward many other syndromes including UBE3A Duplication and Prader-Willi Syndromes. The results could lead to future therapy options in humans.

105.029 29 Using Drosophila to Discover the Biological Significance of Rare Variants Linked to ASDs. S. Mehta*¹, K. Pappu², P. K. Patel² and L. Zipursky², (1)*Semel Institute/UCLA*, (2)*HHMI/UCLA*

Background: The number of ASD candidate genes has increased greatly in recent years with the completion of high resolution CNV analyses on simplex and multiplex families. That number is likely to increase further as genome sequencing efforts on patients with ASDs reach completion. However, there has been a lag between the identification of these candidate genes and our understanding of the pathophysiology of ASDs that is due to our ignorance of the biological functions of many of these genes. Although

simplex cases of ASDs have been shown to have a higher burden of rare variant CNVs, identifying which variants are causal in ASDs cannot be done computationally. For a few candidate genes, the use of animal models has been informative, but it is impractical to make mouse models of all of the ASD rare variants. The fruit fly, *Drosophila melanogaster*, is a well characterized genetic model organism that has previously been used to gain insight about human diseases, particularly neurodegenerative disorders and cancer. The low cost, short generation time, and ease of genetic manipulation make *Drosophila* an ideal system for examining the biological functions of many ASD candidate genes as well as assessing the biological impact of human disease variants.

Objectives: We aim to show that *Drosophila* can be used to effectively study the functions of ASD candidate genes from the standpoint of neural development rather than behavior. To accomplish this, we have chosen to study Neurexin IV (the *Drosophila* homolog of a highly penetrant ASD candidate gene, CNTNAP2) as a proof of principle. We will assess the impact of four evolutionarily conserved rare variants (missense mutations) in Neurexin IV that are linked to cases of Autism.

Methods: We have generated a molecularly defined loss of function allele of Neurexin IV that can allow us to selectively remove Neurexin IV in select populations of neurons. We have also generated transgenic flies that have ASD related variants of Neurexin IV and will assess their function in a Neurexin IV mutant background.

Results: Each of the missense mutations fails to rescue lethality associated with loss of endogenous Neurexin IV despite being made at physiological levels. Several of the mutations result in mislocalization of Neurexin IV, suggesting that these mutations prevent Neurexin IV from binding to its correct partners.

Conclusions: The missense mutations in Neurexin IV associated with ASD significantly impair Neurexin IV function. Given that loss of CNTNAP2 is associated with a familial form of ASD, our work provides evidence that the rare variants associated with CNTNAP2 play a causal role in the development of ASDs. We estimate that about 60% of current ASD candidate genes have a high degree of evolutionary conservation

between humans and *Drosophila*. Based on our experiences studying Neurexin IV, *Drosophila* can be used to effectively probe the biological function of many ASD candidate genes and thereby increase our understanding of ASD pathophysiology.

Epidemiology Program

106 Epidemiology

106.030 30 Early Signs of Autism Spectrum Disorder (ASD) in China. X. Zhang*, *Tianjin Medical University*

Background: In China, diagnosis of autism is mainly based on DSM-IV and medical professionals' clinical experience. To date, there have been few studies on the early signs of autism in mainland China. In this study we tried to estimate the prevalence of ASD among 18-36 month old Chinese children. Then we tried to find out how many items were failed by autistic children and how predictive each item would be for autism. Our goal was to know more about psychological and behavioral development in autistic children and to pave the way for early identification and early intervention.

Objectives: To estimate the prevalence of autism spectrum disorder (ASD) among 18-36 month old children in the Tianjin municipality of China, and to identify early signs of autistic children and how predictive each symptom will be.

Methods: 8000 children aged 18-36 months were screened using a multi-stage stratified sampling procedure and questionnaire based on the Checklist for Autism in Toddlers (CHAT) modified to include early signs of autism. Then we followed the 367 at-risk children and 22 were identified as having ASD on the basis of the Childhood Autism Rating Scale (CARS) and DSM-IV. Discriminant function analysis was performed between ASD children, children not followed up on (group A) and children followed up on but not meeting ASD criteria (group B) to identify early signs of autistic children.

Results: The prevalence of ASD among 18-36 month old Chinese children was 27.5 per 10,000. Items addressing social interaction and communication, e.g. pointing with finger, gaze monitoring, eye contact, age of first smile, interest in peers, obedience to simple instructions,

spoken language had higher weight than other items to distinguish autistic children from both group A and group B. Autistic children showed significant differences from group A, but not group B on pretend play, functional play, and showing and reading parents' facial expressions.

Conclusions: The prevalence of autism spectrum disorder found in our study is lower than the results from previous western studies, but higher than the former study in the same region. Autism has its specific symptoms, such as deficits in social awareness, social relatedness, and social referencing.

106.031 31 Implementation of A European Protocol for Autism Prevalence. A. M. Boilson*¹, A. Staines¹, A. Ramirez² and M. R. Sweeney¹, (1)*Dublin City University*, (2)*The Hope Foundation*

Background: No national prevalence data exists on rates of autism spectrum disorder (ASD) in Ireland. ASD prevalence estimation is complex due to the complexity of case definition and many different protocols have been used in Europe making comparisons difficult. The European Protocol for Autism Prevalence (EPAP) was funded by DG-SANCO to develop a standard protocol for estimating the prevalence of ASD in Europe.

Objectives: To operationalize the European protocol in Ireland and examine the score distribution of the Social Communication Questionnaire (SCQ: Rutter et al., 2003) in a school based population.

Methods: A protocol was developed to screen children for ASD in a school based setting in Ireland. We screened (n = 8,168) children aged 6-11 years, in national (n = 7951, 97%) and special education (n = 217, 3%) schools in three urban regions Galway, Waterford and Cork using the SCQ. A study booklet completed by parents of eligible children capture demographics, and developmental history. Psychological assessments were reviewed and abstracted at psychological services for children with parent reported diagnosed learning disabilities. Clinical data abstracted for children with a confirmed diagnosis of ASD included: cognitive, speech and language, occupational therapy and gold standard ADOS, ADI-R assessments. A validation study of the SCQ was undertaken among a sample of (n =

300) children (6%) of the total population screened who obtained scores in the normal range, and all those who had scored 12 and over.

Results: Completed study booklet returns (excluding incomplete data) from parents for eligible children were as follows: national (n = 5433, 68%) special education schools (n = 72, 33%). The distribution of SCQ scores was highly skewed towards lower scores, 91.6% of children scored in the normal range SCQ Total Score < 12. The Mean score was (4.65) (SD = 4.75) (median = 3.0). There were statistically significant differences in scores by gender (t(5380) = 7.513, p < 0.001); age (F(2, 5457) = 3.582, p = 0.028) and nationality (t(956.017) = - 3.676, p < 0.001). Parents of children who reported diagnosed disorders obtained the highest scores (Mean = 9.12, SD = 7.73) children with no parent reported developmental difficulties (Mean = 3.88, SD = 3.78). Children identified for second stage screening were those scoring 12-14 (n = 225, 4%) and over 15 (n = 231, 4%) on the SCQ.

Conclusions: Implementation of this protocol demonstrates the feasibility of screening children for autism spectrum disorder in an education based setting owing to the overall high response rate (67%) which compares favourably with previous school based studies (29%) (Baron-Cohen et al, 2009). In the current study parent reported diagnosis were validated from multiple clinical sources. The distribution and range of scores was similar to the findings from previous sample community based studies (Chander et al., 2007; Mulligan et al., 2009). Analysis of the results of this study is ongoing.

106.032 32 Inter-Pregnancy Intervals and Risk of Autism in a Population-Based Study. L. Allerton, M. J. Maenner and M. Durkin*, *University of Wisconsin-Madison*

Background: Numerous studies have found associations between perinatal factors and an increased risk for autism. While some factors, such as pre-term birth or low-birth weight, are not clearly controllable based on current knowledge, other reported risk factors may be modifiable. A large and recent study of children from California reported a three-fold increased risk of autism for second-born children whose mothers became pregnant within 12 months after having a previous child, compared to children conceived at

least 36 months since their mother last gave birth.

Objectives: The aim of this study was to evaluate the relationship between inter-pregnancy intervals (IPIs) and autism risk in a population-based cohort of Wisconsin children. If the finding that shorter IPIs substantially increase the risk of autism in second-born children is confirmed, this would strengthen the case for a potentially modifiable risk factor for autism.

Methods: The Wisconsin site of the Autism and Developmental Disabilities Monitoring (ADDM) Network performed a population-based surveillance among 8-year-old children in 2002, 2006 and 2008. Autism case status was determined through the review of medical records by experienced clinicians. Birth certificate information for the autism cases was compared to that for all children born in the same regions of Wisconsin for the birth years corresponding to the cases. Additionally, for comparability with the California study, the analysis was restricted to second-born children who were not multiples, yielding a final sample size of 154 children with autism, and 31,561 controls. IPIs were calculated as the interval between births of the first and second-born, minus the gestational age of the second-born child. This sample had 80% power to detect an odds ratio of 1.7 for autism between the shortest and longest IPI categories. Multivariable logistic regression was used to determine the odds of autism among second-born children in various IPIs. The covariates included in the model were birth year, sex of child, maternal age, paternal age, maternal education, and maternal race.

Results: Among second-born children, the risk of autism among those with IPIs <12 months was not significantly different from children with IPIs ≥ 36 months (OR=1.2, 95% Confidence Interval: 0.79, 1.91). After adjusting for confounding variables, this OR increased to 1.6 (95% Confidence Interval: 0.97, 2.60). While IPIs were not statistically significant predictors of autism, later year of birth, male sex, and white race were associated with increased odds of autism.

Conclusions: We were unable to replicate the finding that shorter IPIs increase the risk for autism among second-born children; if an association is present in this sample, it is likely

much smaller in magnitude than what was previously reported in the literature. Additional studies are needed to clarify whether pregnancy intervals are independent risk factors for autism.

106.033 33 Analysis of Two Polymorphisms On the Serotonin Transporter Gene and Their Interaction with Environmental Stressors During Pregnancy. P. Hecht*¹, M. Tilley², K. L. Jones¹ and D. Q. Beversdorf¹, (1)University of Missouri, (2)Central Methodist University

Background:

While genetics has been shown to have a strong influence in the etiology of Autism Spectrum Disorder (ASD), other factors must also contribute to this disorder. Our previous research has shown a significant increase in prenatal stress in mothers of children with ASD with a peak at weeks 21-32 of gestation. However, not all mothers that encounter stressful situations during pregnancy have children with ASD. It is possible that genetics may play a role in stress tolerance in the development of ASD. The serotonergic system holds particular interest in this regard. The serotonergic system has been implicated as a possible contributing factor to the development of ASD. Moreover, an insertion/deletion polymorphism in the promoter region of the serotonin transporter (5-HTT) gene, SLC6A4, has been associated with anxiety and stress reactivity, and some studies have suggested an association with ASD in carriers of the short allele. Additionally, the 3' polyadenylation site of the serotonin transporter has been shown to have a polymorphism that has a stronger association with panic disorder than the insertion/deletion polymorphism in the promoter.

Objectives:

Our aim is to discover which of these stress-reactive polymorphisms found on the serotonin transporter gene may interact with environmental stressors during the pregnancy to produce a higher risk for the development of ASD in the child.

Methods:

Blood was collected from families with children diagnosed with ASD for genetic analysis. DNA was

isolated using 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.

Results:

Early evidence suggests that the 44 base-pair deletion in the 5-HTTLPR is the critical polymorphism interacting with environmental stressors to increase the risk for ASD in the developing child. Mothers with the 5-HTTLPR short allele have higher numbers of stressors and stressor severity during pregnancy, predominantly during the critical period of pregnancy identified in our previous work, when compared to carriers of the long allele. Furthermore, when compared to the polyadenylation polymorphism, the short allele in the 5-HTTLPR is associated with more stressors and stress severity.

Conclusions:

This study is beginning to suggest a gene and environment interaction in the development of ASD. Our study continues to show the significance of stress during gestation in the etiology of ASD particularly during weeks 21-32. More importantly, this evidence further identifies a specific potential gene that appears to interact with prenatal stress exposure in association with this risk. While the polyadenylation site is linked with panic disorders it does not appear to be interacting with environmental stressors to increase the risk for ASD in the child. Further analysis needs to be conducted to completely understand this gene and environment interaction.

106.034 34 Prevalence and Demographic Characteristics of Children with ASD in A Venezuelan Population. J. A. Chacin*¹, E. Medrano², Z. Gonzalez², V. Toledo², E. Solís¹, A. Costagliola¹ and C. Montiel-Nava¹, (1)*La Universidad del Zulia*, (2)*Hospital de Especialidades Pediátricas*

Background:

Autism is a complex neurodevelopment disorder characterized by deficits in social, language and repetitive behaviors with restricted interests. Recent studies indicate that 1 in 88 individuals have autism. The etiology of autism is unknown, but is considered the most genetic neurodevelopment disorders. Clinical heterogeneity is one reason that difficult to find genes responsible for autism and one of the ways to achieve dimensions is established

Objectives: The aim of this study is to determine demographics characteristics of a population affected with autism spectrum disorder of Maracaibo.

Methods: the sample was constituted for children who attended the human genetic clinic and were born between the years 2000-2004, and at the time of assessment were residents of Maracaibo county; and had a confirmed diagnosis of autism spectrum disorders All children underwent a neurogenetic evaluation to identify medical conditions and/ or genetic syndromes comorbid to the ASD. In order to identify dysmorphic features, neurological abnormalities, and signs of neurocutaneous disorders, a translation of the neurogenetic evaluation form used for AGRE was used. Each child had a complete physical examination, including a neurological examination, an assessment for dsymorphic features, overt physical abnormalities, neurological or motor abnormalities. Karyotyping was performed, and also tests for other genetic syndromes (including Fragile X). During the interviews a detailed medical and developmental history was also obtained, which questioned specifically for non-psychiatric medical illnesses, neurological disorders, medications taken, and treatment responses.

Results: A total of 148 patients were studied, which is equivalent to a frequency of 1 case per 1000 live births. 111 (75%) were male and 37 (25%) female. 136 (91.89%) patients had idiopathic disorder, while 12 (8.10%) had an associated genetic syndrome. The 3 most frequent reasons for consultation were: low social interaction 131 (88.51%), language disorder 140 (94.59%) and stereotyped movements 93 (62.83). The average age of parents at the time of conception was 33 years and mothers 29 years. 85 patients (57.43%) had a family history of

related diseases. Risk factors identified in this sample are age and parental, location in the number of pregnancies and history of affected relatives.

Conclusions:

The estimation of the frequency of ASD in Maracaibo County of 1 child per 1000 live birth might be an underestimation, and a function of the ascertainment process used in this study; since it is a clinical sample. However, results are similar to those reported in other epidemiological studies from other countries. These results are an important contribution to the literature of ASD in Hispanic populations.

106.035 35 Maternal Cholesterol and Autism. J. B. Roulet^{*1}, A. Tsai¹, E. Tierney², H. Gray¹, H. Austin³, B. Wilmot¹ and R. D. Steiner¹, (1)*Oregon Health & Science University*, (2)*Kennedy Krieger Institute*, (3)*University of Colorado Denver*

Background: Several lines of research point to a role for cholesterol metabolism in the pathogenesis of autism spectrum disorders (ASD). First, children with Smith-Lemli-Opitz syndrome (SLOS), a genetic defect in cholesterol synthesis, have a high prevalence of ASD. In addition, a recent study found plasma cholesterol levels were below the 5th percentile in 19% of children with ASD, showing an increased risk for ASD in children with low plasma cholesterol levels but without SLOS. The association between cholesterol and autism is not surprising considering that cholesterol is important for many processes in the developing brain including patterning of the forebrain, neuronal growth and survival, as well as synapse formation. Several studies in animals and humans have shown that maternal cholesterol contributes to the fetal cholesterol pool and fetal steroidogenesis, at least early in embryonic development. Further, low maternal cholesterol levels are associated with adverse birth outcomes and maternal sterol gene variation predicts preterm delivery. Finally, preterm delivery is a risk factor for ASD, and maternal sterol genes predict cholesterol concentration in newborns. Thus perturbations in maternal cholesterol metabolism, especially cholesterol deficiency, may be a risk factor for ASD in the offspring.

Objectives: The objective of the study was to determine if maternal plasma cholesterol concentration is a predictor of ASD in the offspring with the hypothesis that cholesterol deficiency is a risk factor for ASD.

Methods: The study was conducted at 3 institutions: Oregon Health & Science University, Kennedy Krieger Institute and University of Colorado Medical Center. Study participants were recruited among mothers of children with ASD participating in the Autism Treatment Network, excluding individuals with treated/untreated dyslipidemia, diabetes mellitus or other major chronic illnesses. Blood was collected in the morning after an overnight fast and plasma cholesterol concentration was measured. Dietary intake was assessed using the Adult Block food frequency questionnaire.

Results: Eighty five (n=85) subjects were recruited (36.4±6.6 years of age, mean ± SD; ranging from 20 to 52). BMI was typical of U.S. women's (27.1 ± 6.3 on average with 42% normal; 31% overweight, 27% obese). Dietary intake was also typical with 1,719±746 cal/day (15% protein, 38% fat, and 47% carbohydrates), relative nutritional deficiencies in calcium and iron (80% and 81% below DRI for calcium and iron respectively) as well as folic acid (98% were below DRI). Cholesterol intake was 218±107 mg/day with only 20% of the participants above 300 mg/day. The average plasma cholesterol concentration was 174.6±33.3 mg/dl. However 20% of the participants (mothers of children with ASD) were below the 5th percentile for cholesterol levels. No significant relationship was observed between maternal cholesterol concentration or dietary cholesterol intake and any of the offspring's ADOS scores (Communication, Social Interaction, Stereotypy/Aggression).

Conclusions: Mothers of children with ASD have low plasma cholesterol concentrations. These data suggest that maternal cholesterol deficiency is a risk factor for autism.

106.036 36 Late Prematurity and Birth History in Children with Autism. A. Darcy Mahoney^{*1}, B. Minter², M. Higgins³ and K. Burch⁴, (1)*Emory University Nell Hodgson Woodruff School of Nursing*, (2)*Marcus Autism Center- Children's Healthcare of Atlanta*,

(3)Emory Unveristy Nell Hodgson Woodruff School of Nursing, (4)Emory University

Background: The prevalence of children with autism spectrum disorders (ASD) has increased over the past two decades. Major advances in the field of autism include early screening for children with ASD and those considered high risk for the disorder. Over this same time period, the number of infants born preterm has also increased, mostly among those classified as late preterm [LPT] (34-36 weeks gestation). These infants account for 70% of the preterm birth in the US. Vulnerability to a resulting neurobiologic issue, such as the development of ASD, by LPT infants is suspected but has not been well studied.

Objectives: This study explored the relationship between late prematurity, birth history, and autism. The overall objective was to discern whether LPT infants carry the same risk for ASD as full term infants in a retrospective cohort analysis of patients from the Marcus Autism Center.

Methods: With the aim of estimating the probability of autism in LPT children, a retrospective cohort analysis of 664 children was undertaken to look at gestational age, ASD, and birth history. In order to estimate the probability of autism in the LPT population, Bayes' Rule was used. Three pieces of information were necessary to estimate this probability: (1) The overall probability of autism in all children (CDC); (2) Overall probability of the proportion of children born LPT (National Center for Health Statistics); (3) The proportion of late prematurity among autistic children. The first two pieces of information were treated as "population parameters" since this data is obtained from Published National Population Estimates. The third parameter was estimated from the 664 children from the Marcus database in this study.

Results: Our sample of children included 664 patients: 498 were term, 47 were early preterm (EPT), 92 were LPT, and 27 infants were post-term. Of these 21% of the population was female and more than half identified themselves as a minority: African American (34.1%) or Other (19.8%). There were 405 children diagnosed with an ASD in the sample as a whole. Consistent with the literature, our data revealed EPT children have

nearly 2 times the risk of an ASD diagnosis when compared to Term Children ($P < .05$). Late Pre Term (LPT) children have 1.2 times higher risk of an ASD diagnosis when compared to Term Children – this was not statistically significant at $p=0.05$. However, when considering all children in sample who were referred for ASD testing, the relative risk ratio is 1.6 times higher than Term children and this was statistically significant at $p=0.05$.

Conclusions: There is a paucity of evidence regarding the neurodevelopmental outcomes of the LPT children during early school age years. At 35 weeks gestation, the infant's overall brain weight is only 60% of term weight. Because of this anatomical and pathophysiological finding, it is extremely important that we improve our understanding of brain development in the last few weeks of gestation and identify risk factors that may lead to the development of ASD in the LPT infant.

106.037 37 Characteristics of Autism Spectrum Disorder Surveillance Cases without a Community Diagnosis: Missouri Autism and Developmental Disabilities Monitoring Network, 2006-2008. R. Fitzgerald¹, E. Molloy*² and J. N. Constantino¹, (1)Washington University School of Medicine, (2)Washington University in St. Louis

Background: The Autism and Developmental Disabilities Monitoring (ADDM) Network is population-based surveillance system that identifies children with autism spectrum disorders (ASD) in multiple areas of the United States by reviewing evaluations (from birth through 8 years of age) contained in medical and/or educational records of children in a defined population. The ADDM methods do not require a documented diagnosis of ASD to assign an ASD case status, therefore some ADDM ASD cases do not have a documented ASD diagnosis in their surveillance record.

Objectives: To characterize Missouri ADDM surveillance ASD cases without a documented ASD diagnosis.

Methods: The Missouri ADDM site's surveillance area consists of 5 counties in the metropolitan St. Louis area. This analysis was limited to Missouri (MO) ADDM ASD cases from surveillance years 2006 and 2008. We created a dichotomous

variable indicating whether or not an ASD case had a documented ASD diagnosis by a community provider. Univariate analyses were conducted to compare ASD cases with and without at community ASD diagnosis on various demographic, surveillance, and diagnostic variables. A χ^2 test was used for categorical variables. The Wilcoxon Scores test was used to compare distributions of continuous variables for the two groups. We created a logistic regression model to generate adjusted odds ratios for select variables.

Results: A total of 678 8 year-old children met the MO ADDM case definition for. 124/678 (18.2%) of these cases had no abstracted community diagnosis. Only 66/124 (53%) had any mention of ASD on an abstracted evaluation. There were no differences between ASD cases with a community diagnosis vs. those without on gender, race, age at first evaluation, presence of general developmental delay or social delay before 36 months. Cases without a community diagnosis were more likely to have fewer abstracted evaluations (median of 3 vs. 5, $p < .0001$), a comorbid ADDM classification of cerebral palsy (CP) (7.3% vs. 2.0%, $p = 0.002$), and an ASD-NOS rather than Autism ADDM case classification (32.3% vs. 21.7%, $p = 0.012$). ADDM cases without a community diagnosis were also less likely to have a developmental language ($\chi^2 = 8.089$, $df = 1$, $p = 0.005$) or play delay ($\chi^2 = 4.100$, $df = 1$, $p = 0.043$) documented before the age of 3 years. The final logistic regression model (modeling probability of no community diagnosis) contained the following variables: age at first eval (OR = 0.984, 95% CI, 0.973, 0.994), number of abstracted evaluations (OR = 0.830, 95% CI, 0.766, 0.900), co-morbid cerebral palsy (OR = 3.964, 95% CI, 1.541, 10.200), documented regression (OR = 0.461, 95% CI, 0.256, 0.831), and presence of language delay prior to 3 years (OR = 0.547, 95% CI, 0.333, 0.899).

Conclusions: Nearly 20% of MO ADDM ASD cases did not have a documented community. The odds of having documented regression or a language delay before 3 years were approximately 50% less for ASD cases without a community diagnosis suggesting perhaps less severe ASD symptomology. Additionally, the odds of co-morbid CP was nearly 4 times higher for cases without a documented diagnosis. This suggests

that ASD may be under-diagnosed in children with other developmental disabilities like CP.

106.038 38 Verbal and Pragmatic Performance in Children with EARLY Symptoms of Autism. A. Jokel*¹, E. Armstrong², M. Aldridge³, J. Lougeay³, R. Stillman³, L. Gabis⁴ and T. T. Bower³, (1)Tel-Hashomer, Safra Children's Hospital, (2)Texas Woman's University, (3)UTD, (4)Tel Aviv University

Background: Parents and professionals often wonder about language outcomes for young children with autism. At this time, however, there is no consensus on language outcomes for this population. It is still unknown what percentage of children with early symptoms of autism who are not using verbal language to communicate at age 3 (i.e., who are nonverbal) will continue to be nonverbal later in middle childhood and young adulthood. As little as 15 years ago, Bailey, Phillips and Rutter (1996) predicted 50% of children with autism do not acquire useful language, an estimation that is still cited by many researchers and professionals, yet lacks any supporting empirical evidence. Determining verbal outcomes for these children can be complicated because researchers characterize language outcomes in different ways, such as the ability to use useful language or the ability to talk.

Objectives: The current research investigated language outcomes of children who presented with symptoms of autism in the first few years of life.

Methods: The study included 75 children (age range from 6-24 years) who presented with language delays and symptoms of autism between 2 and 3 years of age and who attended a communication program at a university clinic. Participants were recruited by telephone. Standardized and nonstandardized language measures were administered to a subgroup of participants upon follow-up.

Results: Findings revealed that the majority (81%) of children who presented with severe language delays and symptoms of autism in the first few years of life use verbal language by the time they reach school age. Of the 75 children, 53 (71%) were eventually diagnosed with an autism spectrum disorder. Thirty children with an autism spectrum diagnosis and who were reported to be verbal communicators by their parents were

selected for follow-up testing. Results revealed that 37.5% scored within the normal range on the CELF-4 standardized assessment of language and 62.5% scored below the normal range. At the same time, while all these children had a diagnosis on the autism spectrum, not all of them demonstrated pragmatic difficulties as measured on the CELF-4 pragmatics scale.

Conclusions: The majority of the children were found to use verbal language as their primary mode of communication. Language measures demonstrated the variability that characterizes language performance for children on the autism spectrum. Some children scored within the normal range on the standardized measure and yet were not communicatively competent. At the same time, other children scored well below the normal range and yet were able to communicate. Case studies will be presented.

106.039 39 Using Questionnaires to Predict Serum Levels of Polybrominated Diphenyl Ether (PBDE) and Polyfluoroalkyl Compounds. X. Wu¹, D. Bennett¹, D. J. Tancredi², R. J. Schmidt*¹ and I. Hertz-Picciotto³, (1)UC Davis, (2)UC Davis School of Medicine, (3)UC Davis M.I.N.D. Institute

Background:

Polybrominated diphenyl ethers (PBDEs) and polyfluoroalkyl compounds (PFCs) have been widely used in industrial applications and consumer products. PBDEs are used as flame retardants in many household items, such as furniture, electronics, fabrics, and carpeting. PFCs are used in water- and stain-resistant coatings for textiles, oil-resistant coatings for food packaging and cookware, fire-fighting foams, paints, waxes and polishes. They do not easily degrade in the environment and have relatively long half-lives in the body, and have been concerns in regard to the toxicity in the liver, endocrine system, neurodevelopment, immune system, and reproductive system.

Objectives:

Given concerns over their potential adverse health effects, it is of interest to understand personal exposure to these compounds, especially among the sensitive group of young children and women of childbearing age, and to determine alternative

predictors of exposure. This study explored the possibility of predicting serum concentration of PBDEs and PFCs with questionnaire responses on factors including housing characteristics, food intake, and use of consumer products.

Methods:

Between 2008 and 2009, serum samples were collected from three age groups of population in California: young children (2-8 years old; N=67), parents of young children (<55 years old; N=90), and older adults (≥55 years old; N=59). A number of PBDE congeners and six PFCs were measured. A questionnaire collected information on possible predictors.

Results:

Several housing factors were associated with PBDE serum concentrations. Specifically, higher house values were associated with lower serum concentrations; renters had higher serum concentrations than homeowners; and participants living in houses built after 1977 had higher BDE-209 serum concentrations. Associations with home value and renters may reflect socioeconomic differences. However, housing variables were not significantly associated with the change of serum PFCs.

Intake of some food items was associated with elevated serum concentrations of certain PBDE congeners and PFCs, including canned meat (BDE-47, 99 and 154), meat entrees (BDE-209), tuna and white fish (BDE-153, PFDA), dairy fat and freshwater fish (Me-PFOA-AcOH), crackers and microwaving popcorn (PFOS), and marginally for pork and French fries (PFOA).

For consumer product use, we observed significantly higher concentrations of PFOS and marginally significantly higher concentrations of PFDA, PFOA and PFHxS for participants wearing stain-repellant clothes ≥1 time/week, and marginally higher concentrations of PFOS for those wearing waterproof clothes ≥1 time/week. Higher concentrations were observed among people having used fire extinguishers and people with occupational exposure, such as polishing and coating, than among other persons. No correlation was observed with the use of non-stick cookware

or the use of stain-repellant for carpet or furniture.

Conclusions:

A number of significant predictors of serum concentrations of PBDEs and PFCs were identified through the current questionnaire, however, the fairly low R-square of the prediction model indicates unknown contributors, suggesting current questionnaire may not sufficiently predict personal exposure to these compounds; additional measurements are necessary.

This work has been supported by a Cooperative Agreement from Autism Speaks, U.S. Environmental Protection Agency, and Centers for Disease Control and Prevention.

106.040 40 The Early Life Exposures Assessment Tool (ELEAT) for Autism Spectrum Disorders. C. Walker*¹, D. J. Tancredi², D. Bennett³, A. Halladay⁴, R. Butler⁴ and R. J. Schmidt⁵, (1)*University of California at Davis*, (2)*UC Davis School of Medicine*, (3)*UC Davis*, (4)*Autism Speaks*, (5)*UC Davis MIND Institute*

Background: Little is known about the non-genetic, potentially modifiable causes of autism spectrum disorders (ASD) and progress is hindered by the lack of standardized, valid, reliable and inexpensive instruments for assessing the role of candidate environmental exposures.

Objectives: We propose to expand the evaluation of environmental factors in the context of ASD by developing a validated instrument, the Early Life Exposure Assessment Tool (ELEAT), which can be used to assess environment in studies of autism.

Methods: We are in the process of developing, refining, validating, and testing the reliability and feasibility of a self-administered questionnaire to be completed by parents with respect to health and environmental exposures in time windows that are relevant to ASD.

Results: We systematically reviewed the literature to identify ASD-relevant exposure domains with the potential for reliable and valid assessment in a self-administered parent survey. We selected items corresponding to these domains, with preference given to previously validated items, and grouped them into modules –

diet / lifestyle, home environment, and maternal conditions / medical interventions - that can be used together or separately. The questionnaire will be piloted on participants in the MARBLES study, and responses will be compared with data previously collected prospectively during gestation to assess the reliability of retrospective recall.

Criterion and construct validity will be based on comparing questionnaire items responses to corresponding environmental measures, biological measures, and medical record data in the SUPERB, MARBLES, and CHARGE studies, respectively. Feasibility-testing of the ELEAT will be conducted in families of the CHARGE and AGRE studies.

Conclusions: With this instrument comes the potential to achieve enhanced sample sizes through administration of standardized instrument modules to broader populations and data pooling. Such a strategy will allow for assessment of relatively rare gestational exposures and interaction effects, including gene-environment interaction. In addition, the open-source availability of this instrument should facilitate collection and sharing of environmental exposure data among ASD investigators working with diverse populations using dissimilar study designs, enabling collaborations that would not otherwise have had the resources and/or expertise for such exploration. As a result, the number of ASD studies able to assess environmental influences of neurodevelopmental compromise would be greatly expanded, bringing us closer to understanding the potentially modifiable environmental contributions to ASD etiology and paving the way to improved prevention and treatment strategies.

106.041 41 Differences in Diagnosis and ASD Severity Between Latino and White Children. A. B. Ratto*¹, L. Turner-Brown² and J. S. Reznick³, (1)*University of North Carolina-Chapel Hill*, (2)*University of North Carolina at Chapel Hill*, (3)*University of North Carolina - Chapel Hill*

Background: Ethnic minority children are at an increased risk for under-diagnosis and delays in diagnosis of autism spectrum disorder (ASD; Jarquin et al., 2011; Mandell et al., 2002) and appear to have more severe symptoms of ASD (Tek & Landa, 2012). Latino children seem to be at particular risk for these disparities, due to language barriers, financial limitations, and

diminished healthcare knowledge (Liptak et al., 2008; Pew Hispanic Center, 2008). Presently, there is little research available on ethnic disparities in ASD.

Objectives: The goal of the present study was to examine differences in diagnostic outcomes and ASD symptom severity between Latino and White children with a diagnosed ASD. It was hypothesized that Latino children would have greater delays in diagnosis and more severe symptoms of ASD. Income and maternal autism knowledge were also hypothesized to be significant predictors of delays in diagnosis.

Methods: Participants included ASD-diagnosed children of Spanish-speaking Latina (n=28) and English-speaking White (n=28) mothers. Mothers completed background questionnaires, the Social Communication Questionnaire (Rutter, Bailey, & Lord, 2003), and the First Year Inventory-Retrospective (Watson et al., 2007), in their primary language. Mothers were recruited from an ASD research registry and ASD parent support and events.

Results: Despite a lack of significant difference in the age at which mothers reported first developing concerns about their child, Latino children were diagnosed later than their White peers on average, at a level approaching significance ($t = -1.93$, $p < .06$). Notably, among Latina mothers greater affiliation with Latino culture was associated with a later age of first concerns ($F = 5.07$, $p < .05$, $R^2 = .16$). There was also a greater delay among Latino children between the time at which mothers reported first having concerns about their child and the time at which children were diagnosed ($t = -2.23$, $p < .05$). Stepwise multiple linear regression analyses indicated that these differences in age at diagnosis ($F = 6.08$, $p < .05$, $R^2 = .10$) and time to diagnosis ($F = 6.38$, $p < .05$, $R^2 = .11$) were better accounted for by household income. Lower current maternal knowledge of ASD was also associated with greater delays in diagnosis ($r = -.31$, $p < .05$).

There were no significant differences in ASD severity as measured by the SCQ or the FYI-R. However, Latino children were significantly more likely to be diagnosed with autism (odds ratio=6.92), as opposed to Asperger syndrome, high-functioning autism, or PDD-NOS ($\chi^2 = 10.10$,

$p < .001$). Household income did not predict diagnostic labels. Furthermore, survival analyses indicated that Latino children spoke their first words ($\chi^2 = 3.11$, $p < .08$) and achieved toilet training ($\chi^2 = 4.54$, $p < .05$) at later ages on average than their White peers.

Conclusions: The results of the present study provide additional evidence of delays in diagnosis among Latino children, which are not attributable to delays in parent concerns. Household income appeared to drive these differences. Despite a lack of difference in symptom severity on standard measures, Latino children were more functionally impaired by ASD. Further research is needed to identify the factors that contribute to ethnically-based delays in diagnosis and functional impairment. Research is also needed to evaluate whether ethnically-based differential item functioning may occur on parent-report measures of ASD.

106.042 42 Effects of Autism Spectrum Disorder On Parental Employment: Evidence From the National Health Interview Survey. B. P. McCall*¹ and E. Starr²,
(1)University of Michigan, (2)University of Windsor

Background:

Both qualitative and quantitative research has demonstrated that caring for a child with developmental disabilities can have significant effects on parental/caregiver employment. Studies report that caregivers may work reduced hours or take jobs with fewer responsibilities to accommodate the needs of their child. However, although caregivers of children having ASD may have been included in past research, ASD is seldom the primary focus of the research, studies are based on limited data in terms of number of respondents, or they draw from national surveys using only one or two years of data.

Objectives:

The purpose of the current study was to determine the pattern of employment among parents/caregivers of children with ASD in the U.S., compared to parents of children without disabilities using the results of the National Health Interview Survey (NHIS) for the years 1998-2011. We analyze the effects of ASD on hours of work in a week and months of work in a year, and

whether the effects vary by background characteristics.

Methods:

The sample includes the parents of 134,997 children without disabilities and 859 children with ASD aged 3 to 17. We estimate linear regression models to investigate the impact of ASD on parents' weekly hours of work and months of work in the previous year. Multinomial logit models are used to investigate the impact of ASD on parents' work status (i.e., no, part-time, or full-time work) in the week before the survey, and whether they work 0, 1-11 or 12 months in the previous year. The estimates adjust for the complex survey design of the NHIS.

Results:

After controlling for numerous background characteristics, we find that relative to having a child with no disabilities, having a child with ASD lowers the number of hours of work per week by 3.78 for mothers ($p < .01$) but not for fathers ($p > .30$). In addition, having a child with ASD lowers the number of months worked in the previous year by .96 months for mothers ($p < .01$) and .61 months for fathers ($p < .01$). Having a child with ASD also increases the probability of not working at all in the week before the survey by .10 for mothers ($p < .01$) but not for fathers ($p > .30$), and increases the probability of not working in the previous year by .06 for women ($p < .01$) and .03 for men ($p < .05$). We also find evidence that the impact of having a child with ASD on parents' work depends on whether or not a spouse is present, the parent's education level, and the age and race of the child.

Conclusions:

To our knowledge, this is the first research that uses a nationally representative sample to analyze the effect of ASD on both weekly hours of work and months of work in a year, and to explore whether the effect varies by background characteristics. Having a child with ASD leads to significant changes in parents' work behavior, especially for mothers.

106.043 43 Findings from an Autism Surveillance Program in Three Regions of Canada. H. Ouellette-Kuntz*¹, H. Coo¹, M. Breitenbach², P. Hennessey³ and P. Jackman³, (1)Queen's University, (2)Department of Education and Early Childhood Development, (3)Department of Education

Background: Studies conducted over the past few decades have revealed substantial increases in the prevalence of autism spectrum disorders ("autism"), but methodological differences make comparison of the findings problematic. Ongoing surveillance is a more appropriate tool for investigating temporal changes in prevalence.

The National Epidemiologic Database for the Study of Autism in Canada (NEDSAC) was established for this purpose.

Objectives: Our objectives were to monitor the prevalence of autism in three regions of Canada—Newfoundland and Labrador, Prince Edward Island (PEI), and Southeastern Ontario—and to explore the impact of factors such as age at diagnosis and differential migration on any changes observed.

Methods: Cases of autism among children were identified through diagnostic centres, schools, and early intervention programs. Prevalence estimates were calculated for each year of the surveillance period (2003-2010 in PEI and Southeastern Ontario; 2003-2008 in Newfoundland and Labrador) and temporal trends were examined by age group (2-5, 6-9, 10-14 years) and sex by fitting log-linear models using the Joinpoint Regression Program. Age at diagnosis was compared for children diagnosed during the first and second halves of the surveillance period to evaluate the impact of this factor on changes in prevalence in the youngest age group. The estimated number of cases that moved into each region after 2003 was compared to the number that moved from the region, died, or had their diagnosis removed to determine whether, collectively, these factors likely resulted in a net increase or decrease in the numerators used to calculate prevalence.

Results: In the final year of the surveillance period, the estimated prevalence of autism per 10,000 children 6 to 9 years of age was 108.0 (95% CI: 94.2-123.3) in Newfoundland and Labrador; 99.9 (95% CI: 76.3-128.6) in PEI; and 162.5 (95% CI: 145.5-180.8) in Southeastern

Ontario. The trend analysis revealed significant average annual percent increases in prevalence for the overall group of 2- to 14-year-olds ranging from 9.7% to 14.3%, but the findings varied by age group and sex: the lowest change observed was 0.9% (95% CI: -2.3-4.2) for girls in PEI, and the highest was 16.5% (95% CI: 12.7-20.4) for 10- to 14-year-olds in Southeastern Ontario. We found no evidence that the growth in prevalence was starting to plateau except among the youngest age group in Southeastern Ontario, but that finding was likely due to methodological issues. There were no significant decreases in age at diagnosis between the first and second halves of the surveillance period, but differential in-migration may have contributed to a small portion of the observed increases in prevalence in Southeastern Ontario and PEI.

Conclusions: The prevalence of autism increased significantly among all age groups, yet the factors we examined accounted for only a small portion of the observed increases. Accordingly, we cannot rule out the possibility of a true rise in incidence, particularly given the lack of evidence of a leveling-off of prevalence in the younger age groups. Continued surveillance is needed to explain observed increases in prevalence.

106.044 44 Sleep Patterns and Quality Among Children with Autism and Their Caregivers in Oman: A Case Control Study. O. Al-Farsi*¹, Y. M. Al-Farsi², M. I. Waly², M. Al-Sharbati², M. Al-Shafae², A. Ouhtit², M. M. Al-Khaduri² and S. al-Adwai², (1)Ministry of Health, (2)Sultan Qaboos University

Background:

The evidence supporting that children with autism spectrum disorders (ASD) and their caregivers suffer from increased risk of sleep disturbances is growing. Nonetheless, results are not consistent with regard to prevalence rates and types of sleep disturbances. In particular, the evidence exploring this topic among Arab communities is almost lacking.

Objectives: To describe sleep patterns ASD children and their caregivers compared to non-ASD children.

Methods:

A case control study has been conducted on 40 ASD children and 40 non-ASD children and their caregivers. Sleep pattern, quality, and disruptions among ASD children have been assessed using a validated and standardized Arabic version of Pittsburgh Sleep Quality Index (PSQI), and Children's Sleep Habit Questionnaire (CSHQ).

Results:

Overall, the mean PSQI for ASD children was higher compared to non-ASD children (5.0 vs. 4.0; P-value 0.05). Compared to controls, ASD children had lesser duration of sleep (6 vs. 7 hours), and higher incidences of sleep disturbances per month (9 vs. 2). The need to take medication for sleep was 7% among ASD children compared to none among controls. Occurrences of bed-time resistance, sleep-onset delay, parasomnia, and day-time sleepiness were more reported among ASD children. The mean scores for CSHQ were higher among parents of ASD children compared to controls (5.3 vs. 44.5, P-value 0.01).

Conclusions:

The study provides suggestive evidence of reduced sleep duration and quality among children with ASD and their caregivers.

106.045 45 No Differences in Early Immunization Rates Among Children with Typical Development and Autism Spectrum Disorders. K. Angkustsiri¹, D. D. Li² and R. Hansen*³, (1)UC Davis Medical Center, (2)University of California Davis Medical Center, (3)The M.I.N.D. Institute, University of California, Davis

Background: The relationship between vaccines and autism spectrum disorders (ASD) has been of great interest to families and health providers.

Objectives: This study compares the immunization practices of preschoolers with ASD and typical development (TD).

Methods: Immunization records were abstracted from 240 (161 ASD, 79 TD) children between the ages of 24.1-54.4 months participating in the Autism Phenome Project from April 2006 to August 2011. Seventy-eight percent were male. We compared immunization rates for the vaccines required by the State of California for children

ages 18 months to 5 years (3 doses of Hep B, 4 DTAP, 4 Hib, 4 PCV, 3 IPV, and 1 MMR). Of note, there was a national HIB vaccine shortage from 2007-2009. Varicella was not included due to the possibility of naturally acquired immunity.

Results: Immunization rates in ASD children were slightly lower than in TD (see Table 1), but this difference was not statistically significant, with the exception of Hep B, where 91.3% of children with ASD had received 3 doses compared to 98.7% of TD ($p=0.024$). These rates were at or above those reported in the 2011 National Immunization Survey (NIS). One (0.6%) ASD child had not received any immunizations. The national rate for children who received no immunizations was 0.8%.

Conclusions: Despite the lack of evidence supporting any causal relation of vaccines to ASD (IOM, 2011) many parents remain concerned and some choose to delay or avoid vaccines. Immunization rates in preschoolers with ASD in our sample were generally lower than TD, although there were no statistically significant differences except for Hep B. Our study, although not designed to specifically address a causal relationship, does not support an association between vaccines and ASD. In most cases, these immunization practices represent behavior during the first 18 months of life prior to receiving an ASD diagnosis. Further study looking at differences in vaccine acceptance during the 4-6 year booster period is warranted, as having an ASD diagnosis may affect parents' attitudes towards future immunization.

| | ASD (n=161) | TD (n=79) | P- value | 2011 NIS |
|-------|----------------|------------|-------------|------------------|
| Hep B | 147 (91.3%) | 78 (98.7%) | 0.024 | 91.1% |
| DTAP | 150 (93.2%) | 78 (98.7%) | 0.110 | 84.6% |
| Hib | 107 (66.5%) | 48 (60.8%) | 0.386 | shortage 2007-09 |
| PCV | 134 (83.2%) | 66 (83.5%) | 0.128 | 84.4% |
| IPV | 149 (92.5%) | 78 (98.7%) | 0.066 | 93.9% |
| MMR | 151 (93.8%) | 75 (94.9%) | 0.99 | 91.6% |

106.046 46 Environment, the Perinatal Epigenome, and Risk for Autism and Related Disorders. J. I. Feinberg^{*1}, M. A. Taub², S. C. Brown³, R. Irizarry¹, K. D. Hansen¹, L. A. A. Croen⁴, I. Hertz-Picciotto⁵, C. J. Newschaffer⁶, A. P. Feinberg¹ and M. D. Fallin⁷, (1)*Johns Hopkins University*, (2)*Johns Hopkins Bloomberg School of Public Health*, (3)*Bloomberg School of Public Health*, (4)*Kaiser Permanente Division of Research*, (5)*University of California at Davis*, (6)*Drexel University School of Public Health*, (7)*Johns Hopkins School of Public Health*

Background: The study of epigenetic variation is an essential complement to conventional genetic disease studies; unlike sequence variation, epigenetic marks are affected by the environment. We report here on preliminary results of a large Epigenome Roadmap project (Fallin, Feinberg PIs) which takes a comprehensive genome-wide approach to understand the interplay between genetics, epigenetics, and in utero environment in birth and early development phenotypes that are important predictors of adverse outcomes generally, and are related to ASD specifically.

Objectives: As a continuation of our pilot study looking at the role of Epigenetics in ASD, we have measured DNAm across the genome in multiple sample types and time points during and after pregnancy from samples contributed by families enrolled in the EARLI study. Our goal is to assess changes in DNAm in mothers over the pregnancy interval, in addition to fathers and children, and correlations between DNAm and parental or child characteristics that may be related to ASD risk.

Methods: Using prospectively collected biosamples and environmental data, we performed genome-wide DNAm analyses on blood, semen, and placenta samples using both the Illumina 450k platform and CHARM 2.1, another array-based genome-wide approach containing over 4 million probes. In the CHARMed group we analyzed 266 blood samples contributed by 90 pregnant women during all 3 trimesters of pregnancy and 6 months post-delivery. These samples were analyzed against control samples (run on CHARM 2.0) from non-pregnant women matched for age and race. A total of 840 samples contributed by EARLI mothers, fathers and children from an additional 170 families were analyzed on the Illumina platform (and 53 samples from the CHARMed group were also run on the Illumina arrays). We first searched for

regions of the genome where DNAm changes over time in mothers, and then looked for regions that are differentially methylated (DMRs) between individuals with and without particular exposures and/or potential ASD risk factors.

Results: We do not see large changes in DNAm in blood within mothers during pregnancy itself; however, we do observe multiple intra-individual changes in DNAm in blood between the pregnancy and post-partum intervals, with the methylation pattern in post-partum samples showing a striking resemblance to the methylation of the matched non-pregnant control group. Additional cross-sectional analyses of pregnancy-interval blood samples revealed DMRs associated with maternal alcohol use during pregnancy. Results of comparisons with a larger array of factors will also be presented.

Conclusions: Our work has allowed us to develop the laboratory pipeline to analyze DNAm in epidemiologic samples across multiple platforms. It appears that DNAm marks in blood are stable throughout pregnancy, which has implications for interpretation of results relating DNAm with potential ASD risk factors and outcomes. We have developed a strategy for identifying differentially methylated regions related to risk factors and outcomes. This strategy is being applied across a spectrum of variables with the goal of identifying epigenetic marks in families affected with ASDs that may relate to environmental risk factors and thus elucidate mechanisms by which these risk factors influence ASD risk.

106.047 47 Co-Existing Conditions in Children with ASD: Evidence From Two Large UK Databases. B. Koshy^{*1}, M. Maskey², F. A. Warnell², M. A. Johnson³, H. McConachie³, A. S. Le-Couteur³ and J. Parr², (1)*Christian Medical College*, (2)*Institute of Neuroscience, Newcastle University*, (3)*Institute of Health and Society, Newcastle University*

Background:

Children with autism spectrum disorder (ASD) have multiple co-existing conditions ranging from learning disability, disorders of sensory perception to psychiatric co-morbidities. These co-existing conditions add a significant burden to the care of children with ASD; estimation of their true prevalence can help in planning services for children with ASD and their parents.

Objectives:

To identify the prevalence and correlates of parent/carer-reported co-existing conditions in children with ASD.

Methods:

Children were included in either a population-based Database of children with ASD living in the North East of England (Daslⁿe), or a research register - the Autism Spectrum Database - UK (ASD-UK). The parent report questionnaire included basic demographic information and the 10 most common co-existing conditions, rated by parents as frequent (problem behaviour present 3 or more times a week), sometimes (present once or twice a week), never or rare, and in the past only.

Results:

Questionnaires were completed by parents of more than 1500 children aged 2 to 18 years. More than half were reported to present four or more types of problems frequently. Habit problems related to sleep and eating, behavioural problems including hyperactivity and temper tantrums, and emotional problems such as anxiety and sensory issues were reported commonly. Unsurprisingly, children with lower language ability and in special schooling had higher levels of reported problems related to sleep, toileting and eating, hyperactivity, self injury and sensory difficulties. However, anxiety and tantrums were reported as frequent regardless of age, ability or type of schooling.

Conclusions:

The high rates of frequent co-existing conditions as reported by the parents add significantly to the overall complexity of bringing up children with ASD. In future work, we will measure the severity and effect of these co-existing conditions on parents' quality of life, and their experience of services available to assist in management. These findings have implications for appropriate support and intervention services for all children with ASD and their parents.

106.048 48 Can We Confirm an Association Between Shorter Interpregnancy Intervals and Autism?. H. Coo*¹, H. Ouellette-Kuntz¹, Y. M. Lam¹, M. Brownell², M. Flavin¹ and L. Roos², (1)*Queen's University*, (2)*University of Manitoba*

Background: Both short and long interpregnancy intervals (IPIs) are associated with adverse perinatal outcomes. A recent study from California (Cheslack-Postava et al., *Pediatrics*, 2011; 127:246-253) reported an increased risk of autism associated with shorter IPIs, particularly those less than 12 months. This association needs to be confirmed in other populations.

Objectives: Our main objective was to attempt to replicate the findings of Cheslack-Postava and colleagues. A secondary objective was to examine whether maternal age, sex, and birth year—using a cutoff of 1998, the year Canada instituted a mandatory folic acid fortification program—act as effect modifiers of the IPI-autism association.

Methods: Records related to Manitoba births between 1988 and 2005 were extracted from population-based administrative datasets at the Manitoba Centre for Health Policy. First- and second-born siblings from the same mother were identified, applying the following exclusion criteria: multiple gestation, pregnancy loss between the first and second sibling, and autism in the first-born. Three case definitions were used, representing increasing probability of true-positive case status: 1) At least one autism code in the Education, Health, or Children's Special Services datasets (the latter contains information on children identified for a Canadian autism surveillance program through a provincial agency that coordinates the provision of services for children with special needs in Manitoba); 2) Two or more codes for autism in one or more of the preceding datasets; and 3) a record in the Children's Special Services dataset. Logistic regression models were fit to estimate the association between the IPI and autism while controlling for other pregnancy-related variables and sociodemographic factors.

Results: A total of 41,066 second-born siblings met the inclusion criteria. Using ≥ 36 months as the reference, the adjusted odds ratios from the models examining main effects increased from Case Group One (n=472) to Case Group Three

(n=142) across all IPI categories, ranging from 1.23 (0.91-1.65) to 1.70 (0.95-3.05) for IPIs <12 months; 1.09 (0.83-1.43) to 1.56 (0.91-2.66) for IPIs of 12-23 months; and 1.06 (0.78-1.44) to 1.30 (0.71-2.39) for IPIs of 24-35 months. The interactions between IPI and maternal age, sex, and birth year were not significant, but the IPI odds ratios derived from those models attained significance within certain strata (e.g. maternal age 30-34 years), particularly for Case Group Three.

Conclusions: While the findings from the main-effects models were not significant, the point estimates and lower confidence limits for the shorter IPIs suggest an association, albeit a weaker one than observed in the California study. The difference in the proportions of our case and comparison groups with an IPI <12 months (2.1%-3.2%) was substantially smaller than that reported by Cheslack-Postava and colleagues (14.4%). Thus, it seems unlikely that the smaller number of cases in our study can explain the discrepant findings; rather, they may be due to differences in the two studies' case groups or to variations in characteristics of the underlying populations that may influence the IPI-autism association, such as ethnic background. Further analyses are planned to explore the potential impact of these differences on the findings.

106.049 49 Socioeconomic Disparities in ASD Screening Outcomes Using the M-CHAT(-R). M. Khowaja*¹, A. P. Hazzard² and D. L. Robins¹, (1)*Georgia State University*, (2)*Emory University School of Medicine*

Background: With its goals to reduce costs and increase accessibility, healthcare reform has become a popular topic of discussion among US citizens. Lower maternal education, a marker for socioeconomic status (SES), has been linked to decreased access to and utilization of healthcare, due to factors such as reduced awareness of health risk factors and prevention initiatives, limited resources, and poor provider-patient communication.

Objectives: As part of a large autism screening study using the M-CHAT(-R), informal observations have raised concerns regarding differences in screen positive rates across families of different SES. In order to better understand healthcare disparities, this study examines whether socioeconomic variables differentially

affect outcome within this multistep screening study.

Methods: The M-CHAT(-R) is a questionnaire used to screen toddlers for ASDs; the Follow-Up Interview (FUI) clarifies at-risk responses. Parents in metro-Atlanta completed the M-CHAT(-R) at their child's 18- and/or 24-month pediatric visits to identify children at risk for autism spectrum disorders (n=11,918). 1,025 (8.6%) screened positive on the questionnaire, 758 of whom were successfully contacted to complete the FUI. A total of 232 were offered a free evaluation after demonstrating continued risk on the FUI. Diagnostic evaluations were completed by 145 families with 82 (57%) resulting in an ASD diagnosis. An additional 6,421 toddlers were excluded from the sample due to missing demographic data (i.e., sex, maternal education, ethnicity), language barrier, significant motor delays that would preclude standardized assessment, or because they were part of a developmentally typical control sample.

Results: Level of maternal education ranged from less than 8th grade to graduate-level education (median was a bachelor's degree, 33% of sample). Among parents who completed the M-CHAT(-R), screening results were significantly related to level of maternal education (i.e., < 8th grade, high school, some college, bachelor's, graduate), $\chi^2(4, 11,918)=213.8, p<.001$. That is, as maternal education decreased, children were more likely to initially screen positive. Among those who completed an FUI, interview results were also significantly related to maternal education, $\chi^2(4, 758)=14.7, p=.005$. Children of families with the highest level of maternal education (graduate level) were more likely to continue to screen positive on the FUI. This suggests that the greatest consistency across questionnaire and interview level of screening is seen in those with the highest level of education. Finally, at evaluation, maternal education was not significantly related to diagnostic outcome, $\chi^2(4, 145)=6.1, p=.194$.

Conclusions: Results suggest that children of parents with lower SES are more likely to initially screen positive on the M-CHAT(-R) than those with higher SES. Screening outcome remains most consistent from questionnaire to interview for those with graduate level degrees, possibly

due to increased awareness of normative childhood development. This also suggests that FUI plays a significant role in reducing the inflated screen positive rate for families of lower SES. At the diagnostic level, SES disparities are no longer apparent, supporting previous findings of consistent ASD rates across diverse backgrounds. Additional research on reasons for these differences is needed in order to eliminate disparities in identification and referrals for intervention.

106.051 51 Heavy Metals and Porphyrin Levels in Autism Spectrum Disorders. M. Macedoni-Luksic*¹, D. Gosar¹, J. Orazem¹, J. Kodric¹, P. Lesnik Musek¹, A. France Stiglic², M. Zupancic¹, A. Sesek Briski², D. Neubauer¹ and J. Osredkar², (1)Univ. Paediatric Hospital, (2)Clinical Institute of Clinical Chemistry and Biochemistry

Background:

While genetic factors are recognized as being important in the pathogenesis of autism spectrum disorders (ASD), a role for environmental factors has received considerable attention. Among environmental factors that may be important in the development of ASD, heavy metals, especially mercury, has been examined most often. A porphyrin pattern in urine of patients with ASD may be one of the signs of the heavy metals toxicity. Despite many studies in the field, well controlled studies, including patients with other neurological diseases, are still very rare.

Objectives:

The aim of our study was to determine the levels of heavy metals in blood (zinc, copper, aluminium, lead, mercury), as well as the specific porphyrin levels in the urine of patients with ASD compared with patients with other neurological disorders.

Methods:

The study was performed in a group of children with ASD (N=52, average age=6,2y) and control group of children with other neurological disorders (N=22, average age=6,6y), matched in terms of intellectual abilities (Mann-Whitney U = 565.0, $p = .595$). Measurement of heavy metals in blood was performed by atomic absorption

spectrometry, while the HPLC method via a fluorescence detector was used to test urinary porphyrin levels. Results were compared across groups using a multivariate analysis of covariance (MANCOVA). In addition a generalized linear model was used to establish the impact of group membership on the blood Cu/Zn ratio.

Results:

In term of heavy metals blood levels no significant difference between the groups was found. However, compared to the control group, ASD group had significantly elevated blood Cu/Zn ratio (Wald $c^2=6.6$, $df=1$, $p=.010$). Additionally, no significant difference between the groups was found in term of Uroporphyrin I, Heptacarboxyporphyrin I, Hexacarboxyporphyrin, Pentacarboxyporphyrin I, Coproporphyrin I and Coproporphyrin III level in urine.

Conclusions:

The higher Cu/Zn ratio may indicate a decrement in metallothionein system functioning, so we suggest to test blood levels of zinc in all children with ASD and give them a Zn supplement if needed.

106.052 52 Training Program in Autism to Primary Care Professionals in São Paulo, Brazil - PILOT Study. D. Bordini¹, C. de Paula^{*2}, R. Lowenthal¹, G. Araujo Filho¹, A. A. Gadelha¹ and J. J. Mari¹, (1)*Federal University of São Paulo*, (2)*Mackenzie Presbyterian University*

Background:

Pervasive Developmental Disorders' treatment early on can be cost effective and lead to improvement on the prognostic and quality of life for individuals later on. However, late identification of Pervasive Developmental Disorders (PDD) is an universal problem and even more complicated in South America.

In Brazil, the Unified National Health System provides universal access to health services for the entire Brazilian population. This system is organized regionally, composed of clinics that integrate primary and specialty care; the Brazilian

mental health system is fully integrated with the Unified National Health System. For the treatment of PDD children and adolescents the main service are the Psychosocial Community Care Centers for Children and Adolescents (CAPSI), while for identification of these cases, the main resource are primary care health clinics. The CAPSI team comprises specialized mental health professionals, but professionals from primary care health clinics don't have training in mental health, neither about PDD, therefore they need to be trained.

Objectives:

This study aimed to evaluate the impact of a training course about autism to pediatricians and other primary care professionals in the north region of São Paulo city in Brazil.

Methods:

The course was conducted in five weekly meetings, 3 hours each: 2 hours of lectures offered by PDD experts, plus 1 hour of case discussion. The main topics were: (1) main symptoms of PDD, (2) epidemiology, (3) instruments, (4) early signs and (5) evidence based treatments for PDD.

The participants were 22 professionals from primary care clinics from the north region of São Paulo city: 17 Pediatricians, 4 General Practitioners and 1 Psychologist. All of them were evaluated before and after training according to a structured questionnaire with 13 questions about PDD knowledge.

Results:

Overall, there was a statistically significant improvement in PDD knowledge after training in comparison to the knowledge before training: mean 6.73 x 8.18 ($p<0.01$). They correctly answered 148 questions before the training, and 203 question, after the training (improvement of 37%).

The results also showed a change in clinical practice: after training: the trained professionals

referred 3 times more suspected PDD cases to CAPSI (4 months after training in comparison to 4 months prior training). In addition, all of the suspect case had clinical symptoms compatible with PDD or sufficiently complex that required a specialized evaluation for differential diagnosis.

Conclusions:

This training course seems feasible, low cost, and able to improve knowledge and referrals among primary care professionals.

This pilot study has several limitations, but can be considered successful, since it reached its main goal: to sensitize primary care professionals to identify suspected cases of PDD and immediately refer them to specialized service (CAPSI) to be better evaluated and adequately treated.

106.054 54 Medical Conditions and Health Care Utilization Associated with ASD in Adulthood. O. Zerbo*, L. A. Croen and M. L. Massolo, *Kaiser Permanente Division of Research*

Background: Children with autism spectrum disorder (ASD) are growing up and becoming adults. However, very little is known about medical conditions and health care utilization patterns among this growing population. Elucidation of these medical care issues is critical to the development of effective strategies for health care delivery to adults with ASD.

Objectives: The objectives of this study are: 1) to describe the prevalence of ASD in adults, 2) to investigate the frequency of medical and psychiatric co-morbidities and utilization of psychotropic and other medications, 3) to describe utilization of health services among adults with ASD, and 4) to assess adult medicine and other practitioners' knowledge about ASD.

Methods: The study population was drawn from the total population of adult members of Kaiser Permanente Northern California (KPNC) as of 2012 (N~2.4 million). We utilized data routinely captured in KPNC electronic clinical databases for all analyses. ASD cases were defined according to International Classification of Diseases-9-Clinical Modification (ICD-9-CM) 299.0; Asperger's Disorder or Pervasive Developmental Disorder Not Otherwise Specified (PDD-NOS) (ICD-9-CM

299.8). Adults without an ASD diagnosis were sampled at a 10:1 ratio and constituted the comparison group. We calculated overall prevalence of ASD, and prevalence by sex, age group (18-24, 25-29, 30-34, 35-39, 40-44, 45-49, 50-54, 55-59, 60-64, 65+), and race/ethnicity (white, Hispanic, African American, Asian, Other). We also calculated the prevalence of psychiatric and medical co-morbidities, and quantified the utilization of primary care, specialty care, and preventive care services overall and by sex, age group, and race/ethnicity. Specific psychiatric and medical co-morbidities examined include: Depression, anxiety, obsessive compulsive disorder, schizophrenia, bipolar disorder, mood disorders, psychoses, diabetes, obesity, cardiovascular outcomes (coronary artery disease, peripheral vascular disease), hypertension, cancer, seizure disorders, insomnia, asthma, allergy, autoimmune diseases, gastrointestinal disorders (e.g. GERD), osteoporosis, chemical dependency, smoking, and alcohol use. For comparisons of prevalence of co-morbidities and utilization of medical care services between adults with ASD and adults without ASD, we used all data recorded in the electronic medical record in the 24-month time period from January 2009-December 2011. To assess provider knowledge about ASD, all adults primary and specialty care clinicians (~1700) were invited to complete a brief online survey (~10 questions, 2 minutes to complete).

Results: The overall prevalence of ASD among adult members of KPNC as of March 2012 was 16/10,000. Prevalence varied by age category, with the highest prevalence in the 18-24 age group (81/10,000). Prevalence also varied by sex, with a male: female ratio of 3 to 1. Further data on the prevalence of medical comorbidities and healthcare utilization will be presented.

Conclusions: The prevalence of ASD in young adults is similar to that of school aged children. The final results from this study will contribute to filling important knowledge gaps in our understanding of the prevalence of psychiatric and medical co-morbidities and patterns of health care service utilization among this vulnerable population. Moreover, results from the provider survey will lead to the development of improved strategies for delivering the most appropriate and effective health care to this growing population.

106.055 55 Epidemiology of Neglect and Maltreatment in Children with Autism Spectrum Disorders. L. B. King*, C. A. Cheely, J. Charles, W. Jenner, J. S. Nicholas and L. A. Carpenter, *Medical University of South Carolina*

Background: Although researchers have speculated that youth with autism spectrum disorders (ASD) are at particular risk for maltreatment due to social and communication impairments, there has been little research examining this issue. One study reported ASD rates of 18.5% and 16.6% for physical and sexual abuse respectively; however this data was centered on caregiver report in a high-functioning sample. Based on an increasing ASD prevalence, it is imperative that we determine the relationship between children with ASD and maltreatment.

Objectives: This research aims to determine the prevalence of neglect and maltreatment among children with ASD, determine the number and type of outside placements, compare findings with a matched control group, and determine risk factors of neglect and maltreatment.

Methods: Information was collected on 8-year old children in South Carolina between 2000 and 2008 as part of an ongoing CDC-sponsored population-based multiple source surveillance of ASD. Data collected included ASD case status, previous diagnosis, Intellectual Disability (ID), and presence of autism discriminators. These data were linked with data from the Department of Social Services (DSS), the lead agency for child protective services and foster care in the state. DSS data included number of cases of maltreatment, number of outside placements, and maltreatment category for founded cases. This data was provided for all children with ASD as well as on a comparison control group that was randomly selected and matched on age, sex, and race, at a rate of 3:1. From the linked dataset, we calculated descriptive statistics for number of founded DSS cases and placements, with Chi-square tests or Wilcoxon rank sum tests used to determine differences between ASD-cases and ASD-non-cases. Logistic regression was used to calculate risk factors of neglect and maltreatment among children with ASD.

Results: Of 873 children with ASD, 115 (13%) were identified in DSS. ASD cases had a mean of 1.4 (SD±0.73) founded cases, compared to 1.9

(±1.3) for non-ASD controls (p=0.001). Reasons for removal of children with ASD were similar to the control group, with the majority removed due to neglect. As children aged and were in the system longer, those with ASD more often reported neglect as the maltreatment code, compared to controls (92% versus 71%, $X^2=4.3$, p=0.04). And although not significant, 12% of ASD cases reported medical neglect, compared to 8% of non-ASD controls.

ID, previous ASD diagnosis, and special education placement were determined to be significant risk factors predicting DSS services. OR was 4.0 for ID compared to non-ID children (95% CI 2.3-7.2), 1.9 for NO previous ASD diagnosis compared to children with prior diagnosis (95% CI 1.1-3.2) and 2.4 for children in an "Other Health Impairment" educational classroom compared to children in other classrooms (95% CI 1.1-5.1).

Conclusions: This research indicates that children with ASD are similar to controls with regards to percent in DSS and maltreatment type, however their need for social services does not decline with age. ASD children with ID, no prior ASD diagnosis, and in a non-autism specific classroom are at highest risk of requiring DSS services.

106.056 56 Obstetric Risk Factors and Autism Spectrum Disorders in Finland. P. Polo-Kantola¹, K. M. Lampi*¹, S. Hinkka-Yli-Salomäki¹, M. Gissler², A. S. Brown³ and A. Sourander⁴, (1)*University of Turku*, (2)*Nordic School of Public Health*, (3)*New York State Psychiatric Institute*, (4)*Turku University Hospital*

Background: Current research suggests that obstetric risk factors occur more in ASD compared to unaffected siblings or matched controls. Although the findings are inconsistent, previous studies have reported associations between ASD and e.g. maternal hypertension or pre-eclampsia, uterine bleeding, threatened abortion, breech presentation, caesarean section and low Apgar scores. Most of these risk factors are likely to represent conditions related to fetal hypoxia. Previous population-based studies examining obstetric risk factors have usually included only cases with infantile/childhood autism or have used a broader definition of ASD. There are very few studies that have examined obstetric risk factors specifically for Asperger's syndrome or PDD.

Objectives: To examine the relationship between obstetric risk factors and childhood autism, Asperger's syndrome and other pervasive developmental disorders (PDD).

Methods: Register-based case-control study from all singleton births in Finland from 1990-2005. A total of 4713 cases with diagnoses of childhood autism, Asperger's syndrome or PDD (based on the ICD-10) were identified from the Finnish Hospital Discharge Register. Each case was matched to four controls on sex, date of birth, and place of birth. Information on obstetric risk factors was obtained from the Finnish Medical Birth Register. Conditional logistic regression models were used for statistical analyses.

Results: When adjusted with possible confounders childhood autism was associated with maternal high blood pressure (OR 1.45, 95% CI 1.0-2.0, P=.032), birth type by vacuum or forceps (OR 0.71, 95% CI 0.5-1.0, P=.043), Apgar scores less than 7 (OR 1.48, 95% CI 1.1-2.0, P=.018) and neonatal treatment with monitoring (OR 1.39, 95% CI 1.0-1.9, P=.045). PDD was associated with induced labour (OR 1.25 95% CI 1.1-1.5 P=.006), planned caesarean section (OR 1.34, 95% CI 1.1-1.7, P=.010), Apgar scores 7-8 (OR 1.22, 95% CI 1.1-1.4, P=.008) and NICU treatment (OR 1.45, 95% CI 1.1-1.9, P=.008), while Apgar scores less than 7 narrowly missed an association (OR 1.30, 95% CI 1.0-1.7, P=.060). Asperger's syndrome was associated only with Apgar scores 7-8 (OR 1.19, 95% CI 1.0-1.4, P=.022).

Conclusions: Low Apgar scores as well as conditions requiring neonatal special follow-up were associated with childhood autism and PDD. These findings suggest that fetal distress is a potential risk factor for these disorders, but not for Asperger's syndrome.

106.057 57 The Association Between Gestational Exposure to Nonsteroidal Anti-Inflammatory Drugs and Autism. T. Tseng^{*1}, M. L. Adams², W. D. Rich², D. Tillman² and I. Hertz-Picciotto³, (1)*Campbell University College of Pharmacy and Health Sciences*, (2)*Campbell University College Pharmacy and Health Sciences*, (3)*University of California at Davis*

Background:

Nonsteroidal anti-inflammatory drugs (NSAIDs) are one of the most commonly prescribed drugs during pregnancy. Specifically, aspirin is given to mothers with high-risk pregnancies and produces a moderate reduction of certain risks, without infant bleeding, including preeclampsia, delivery before 37 weeks of gestation and fetal growth restriction. NSAIDs cross the placenta and the long-term effects on children are unknown. NSAIDs involve cyclooxygenase (COX)-1 and COX-2 inhibition. COX-2 has been shown to play a role in fetal brain development, specifically the dendritic branching involved in the developing areas of the brain that are responsible for cognitive function. The influence of NSAIDs on CNS development is not well understood and furthermore, their potential role in autism has not been studied.

Objectives:

The objective of the study is to identify a possible novel risk or protective factor, gestational exposure to NSAIDs associated with autism.

Methods:

Northern California families were enrolled from 2003 to 2010 in the CHARGE (Childhood Autism Risks for Genetics and Environment) population-based case-control study. Children aged 24-60 months were evaluated and confirmed to have autism (n=357), autism spectrum disorder (ASD, n=163), or typical development (n=371) at the University of California-Davis Medical Investigation of Neurodevelopmental Disorders Institute using standardized clinical assessments (ADOS, ADI-R, Mullen's Scales of Early Learning, and Vineland Adaptive Behavior Scales). The ASD group were those children who met criteria for autism on ADOS and on one of the communication or social domains on the ADI-R, and who were within 2 points of meeting the other cut-off. In our preliminary analysis, we calculated unadjusted odds ratios (ORs) for the association between autism and gestational exposure to NSAIDs (before and during pregnancy).

Results:

Mothers of children with autism were less likely than those of typically developing children to

report having taken NSAIDs during periconception or pregnancy (OR=0.65, 95% CI 0.49-0.88).

Moreover, mothers of children with autism and ASD combined were also less likely than those of typically developing children to report having taken NSAIDs during periconception and pregnancy (OR=0.67, 95% CI 0.51-0.88).

Conclusions:

Our preliminary results may suggest protective relationship between gestational exposure to NSAIDs and autism, but further analysis is underway to address potential confounding or other bias. Nevertheless, this is a large study sample, the exposure is quite common, and relevant biologic pathways deserve further attention, as this relationship may be complex and needs to be further elucidated. If confirmed upon more rigorous analysis, this research may present possible novel inventions for the prevention of ASD and autism.

106.058 58 Elevated Maternal C-Reactive Protein and Autism in a National Birth Cohort. A. S. Brown*¹, A. Sourander², S. Hinkka-Yli-Salomäki³, I. W. McKeague⁴, J. Sundvall⁵ and H. M. Surcel⁵, (1)NYSPI, (2)Turku University Hospital, (3)University of Turku, (4)Columbia University Mailman School of Public Health, (5)National Institute for Health and Welfare

Background:

Autism is a complex neuropsychiatric syndrome with a largely unknown etiology. Inflammation during pregnancy may represent a common pathway by which infections and other insults increase risk for the disorder.

Objectives:

We investigated the association between early gestational C-reactive protein (CRP), an established inflammatory biomarker, prospectively assayed in maternal sera, and childhood autism in the Finnish Prenatal Study of Autism (FiPS-A), a large national birth cohort (N=1.6 million pregnancies).

Methods:

The FiPS-A is based on a nested case-control design. The sampling frame consisted of all

offspring born in Finland from 1987-2005, and subjects were followed up until 2007. All offspring were derived from the Finnish Maternity Cohort, which consists of virtually all pregnancies with archived serum specimens from the first and early second trimesters (one per pregnancy) beginning in 1983. The Finnish Hospital/Outpatient Discharge Registry was used to identify all cases with childhood autism (ICD-10 F84.0). Cases (N=677) were matched 1:1 to controls from the birth cohort who were without ASD or severe/profound mental retardation on date of birth, sex, birthplace, and residence in Finland. CRP was quantified by a latex immunoassay.

Results:

The analysis revealed a significant association between increasing maternal CRP and risk of autism in the offspring (OR=1.12, 95% CI=1.02-1.24, p=.02). There was a greater than 40% increase in risk of childhood autism following exposure to elevated maternal CRP, defined *a priori* as a CRP level in the highest quintile (>5.84 mg/dl), compared to maternal CRP in the lowest quintile (0.10-0.92 mg/dl) (OR=1.43, 95% CI=1.02-2.01, p=.039). We observed an 80% increase in risk of childhood autism following exposure to elevated maternal CRP, defined *a priori* as a CRP level in the highest decile (>9.55 mg/dl), compared to the lowest decile (0.10-0.57 mg/dl) (OR=1.80, 95% CI=1.09-2.97, p=.02).

The findings were not confounded by maternal age, paternal age, number of previous births, maternal socioeconomic status, pre-term birth, low birthweight, maternal/parental history of psychiatric disorders, and gestational week of the blood draw. There were associations between maternal CRP and risk of autism in both sexes, with a numerically greater association for females, but the findings for both sexes fell short of statistical significance (males: OR=1.10, 95% CI=0.98-1.24, p=0.09; females: OR=1.20, 95% CI=0.97-1.49, p=0.10). There was no statistical evidence of interaction between maternal CRP and sex on the relationship with autism (p=0.50).

The relationships were similar for cases with mental retardation (MR) (OR=1.17, 95% CI=0.94-1.45, p=0.17) and without MR (OR=1.11, 95% CI=0.99-1.25, p=0.06).

Conclusions:

Elevated maternal CRP during pregnancy is related to an increased risk of autism in offspring. This exposure may represent a common pathway by which infections, other inflammatory insults, and the cytokine response, elevate risk for autism and these outcomes. The findings are consistent with previous associations between elevations in maternal serum and amniotic fluid cytokines and risk of ASD in offspring. The present investigation may stimulate work on possible molecular mechanisms by which elevated CRP disrupts placental function and alters fetal brain development. These findings may also have important implications for prevention of autism.

106.059 59 Blood Serotonin Levels in Autism: A Systematic Review and Meta-Analysis. S. Gabriele*¹, R. Sacco¹ and A. M. Persico², (1)*University Campus Bio-Medico*, (2)*IRCCS*

Background: Autism spectrum disorder (ASD) is a complex neurodevelopmental disorder characterized by a broad heterogeneity in clinical symptoms and developmental trajectories. Given this complexity, there has been an intensive search to identify biological markers able to aid clinicians in early diagnosis, clinical prognosis and prediction of treatment response. Fifty years ago, elevated blood serotonin (5-hydroxytryptamine [5-HT]) levels, or hyperserotonemia, was identified as a biomarker for autism and it is still one of the most consistent quantitative traits associated with the disease.

Objectives: Many studies on hyperserotonemia have been reported in the literature, measuring differences between samples of autistics and controls. Given the different methodologies used through the years to measure peripheral serotonin, we performed a systematic review and conducted a series of meta-analyses in order to provide an overall estimate of the effect size and significance of the association between hyperserotonemia and autism, as well as to verify whether and to what extent different methodologies have influences this effect size.

Methods: First we searched the Pubmed database using a combination of keywords related to 5-HT and ASD, and reviewed only articles reporting mean and standard deviation values for autistics and controls. We then pooled studies depending on biological substrate (Whole Blood [WB] [values in ng/mL or ng/10⁹PLT]; Platelet-Rich Plasma

[PRP] [values in ng/10⁹ PLT] and Platelet-Poor Plasma [PPP] [values in ng/mL]) or methodological procedures (HPLC or fluorometric assays). Finally, data from each publication were meta-analysed to generate a pooled effect size using a fixed or random effects model, depending on between-study homogeneity or heterogeneity, respectively.

Results: Sixteen studies evaluated 5-HT levels in WB. Meta-analysis on these studies shows significantly higher serotonin levels in autistics compared to controls. An higher effect size has been found by studies measuring 5-HT levels normalized by platelet count (O.R. = 6.7; P < 0.001), as compared to 5-HT values expressed in ng/mL (O.R.= 3.14 ; P < 0.001) even if a substantial between-study heterogeneity was found (P < 0.05). Furthermore, four studies measured 5-HT levels in PRP. No between-study heterogeneity was found (p-value = 0.11), and significantly higher 5-HT levels were found in autistics (O.R.= 2.6; P < 0.001). Only three studies were selected for serotonin levels in PPP. In this case, no significant group difference was observed (O.R. = 0.54; p-value = 0.36) Finally, meta-analyses on studies using HPLC versus fluorometric assays, found a similar effect size on 5-HT measures in autism.

Conclusions: These results confirm a strong overall association between higher levels of blood serotonin with autistic disorder, as repeatedly observed in autism research. In particular, more stringent association was found with ASD when 5-HT assay were performed in WB and PRP, normalized for platelet content. Meta-analyses clearly indicate both as excellent substrates for 5-HT assessment in autism. Moreover, both HPLC and fluorometric assays, result as valid measurement methodologies. However, our study reinforces the role of serotonin as a biomarker in autism, and it could provide indicative elements also for clinical use.

106.060 60 Prevalence of Autism Spectrum Disorders (ASD) Among Young Children, by Demographic Characteristics. G. C. Windham*¹, K. S. Smith², M. Anderson², N. J. Rosen³, L. A. Croen⁴ and C. E. Rice⁵, (1)*California Department of Public Health*, (2)*Impact Assessment, Inc.*, (3)*UC Berkeley SPH (current)*, (4)*Kaiser Permanente Division of Research*,

(5) *National Center on Birth Defects and Developmental Disabilities*

Background: Standardized collection of data for monitoring trends has documented continuing increases in identified ASD prevalence in the U.S. among school-aged children (8-year-olds). Despite concerns about development before the ages of 2- and 3-years, most children are not diagnosed until after age 4 years. Delays in early evaluation and diagnosis create challenges for monitoring ASD prevalence among young children.

Objectives: Establish a multi-source, active surveillance system to determine prevalence and demographic characteristics of children < 48 months identified with ASD in one-county in California for two birth years, 2005-2006.

Methods: Methods are based on those of the Autism and Developmental Disabilities Monitoring (ADDM) network established by the U.S. CDC. Records of children with a diagnosis or signs of ASD at health-related sources (Early Start Programs, CA Department of Developmental Services, Kaiser Permanente Medical Care Program, and clinics) were reviewed and abstracted. An expert review process was followed to determine surveillance case classification consistent with *DSM-IV-TR* criteria for autistic disorder, PDD-NOS, or Asperger's disorder. Both birth and current prevalence were determined. Records were linked to birth certificates to identify resident births and obtain demographic information. Census data for the population of 2 and 3-year olds in the appropriate years were used for current prevalence. Prevalence ratios (PR) and 95% CI were calculated to compare sub-groups.

Results: For 2005 births, 200 children were ascertained as definite cases for a prevalence of 7.6/1000 births (95% CI 6.5-8.6). Prevalence was slightly higher in 2006 at 8.4/1000 births (CI =7.3-9.4). Combining the two years, prevalence was significantly higher among males than females with a PR of 3.7 (CI 2.9-4.7). Prevalence varied by race/ethnicity as well, with a significantly elevated PR among Asians compared to white, non-Hispanics (PR=1.3, CI 1.0-1.7) and slightly elevated among Blacks, although based on small numbers. Prevalence was significantly lower

among Hispanics, particularly among children whose mothers were foreign-born (PR= 0.49, CI 0.36-0.69). Multi-variate modeling and additional sub-group analyses will be conducted.

Conclusions: The identified ASD birth prevalence among young children (<4) is about 75% higher than prevalence in this area among 8-year old children a decade earlier, although case-finding methods differed slightly. Furthermore, although on the low side, rates are within the range of US ADDM Network sites reporting 8-year-old prevalence. These results indicate ASD prevalence can be estimated at younger ages on a population basis and provide evaluation of methods for monitoring at ages less than four.

106.061 61 Analysis of the Ages and Stages Questionnaire 3rd Edition (ASQ-3) Compared to the Modified Checklist for Autism in Toddlers - Revised (M-CHAT-R): An Update. L. D. Haisley*¹, S. Hardy², C. Manning¹, M. Barton¹ and D. A. Fein¹, (1)*University of Connecticut*, (2)*University of Rhode Island*

Background:

Since 2006, the American Academy of Pediatrics (AAP) has recommended developmental screening using a validated screening tool at all well-child visits. The AAP additionally recommended autism-specific screening at 18- and 24-months. Pediatricians note a lack of time and resources as barriers to autism-specific screening. Although some preliminary research has indicated that broad-band screeners may be able to detect autism, at this time there is insufficient data to support using broadband developmental screeners in lieu of autism-specific screeners.

Objectives:

To extend previous study results testing the sensitivity and specificity of both the broadband Ages and Stages Questionnaire (ASQ), and the autism-specific Modified Checklist for Autism in Toddlers- Revised (M-CHAT-R) in detecting autism spectrum disorders (ASDs) amongst children screened at 18- and 24- months.

Methods:

1846 children were screened with the M-CHAT-R and the ASQ. Of those children, 157 failed the M-

CHAT-R. The parents whose children failed the M-CHAT-R were contacted for a follow-up phone interview. Forty-six children failed the phone-interview and were invited to the University of Connecticut for a developmental and diagnostic evaluation. Thus far, 33 of these 46 children have received evaluations. The sensitivity and specificity of the ASQ for detecting children who failed the M-CHAT-R, children who failed the follow-up interview, and children found to have an ASD upon evaluation, was assessed. Data is presented on the specific ASQ domains (Communication, Gross Motor, Fine Motor, Problem Solving and Personal-Social) that children with an ASD diagnosis failed.

Results:

In the following analyses, to fail the ASQ, the child had to fail one or more domain. Among children who failed the M-CHAT-R ($n = 157$), the ASQ demonstrated 52% sensitivity and 89% specificity with the M-CHAT-R screener. Among the children who failed the follow-up phone interview ($n = 46$), the ASQ demonstrated 85% sensitivity and 61% specificity ($\chi^2 = 27.63$, $p < .001$) at detecting the children who failed the follow-up phone interview. In terms of children who received an ASD diagnosis ($n=11$), the ASQ demonstrated 82% sensitivity, and 14% specificity ($\chi^2 = 0.098$, $p = .75$).

Thirty-three children were evaluated and received the following diagnoses: 11 ASD, 11 Developmental Delay, 4 Developmental Language Disorder and 7 No Diagnosis. Eight failed the Communication domain, 5 Personal-Social, 4 Fine Motor, and 3 Problem Solving.

Conclusions:

The ASQ identified 9 of the 11 children who received an ASD diagnosis. Therefore the ASQ demonstrates good sensitivity in identifying children at risk for an ASD. However, the ASQ's specificity is less than that demonstrated by the M-CHAT-R. Therefore, the data corroborate the suggestion to use a broad-based screener in conjunction with an autism-specific screening measure; specifically those children who fail the ASQ, should be given an autism-specific screener. Further analyses will be run on the specific

predictive power of each ASQ domain, and total ASQ scores.

106.062 62 The Familial Factors and Child's Symptomatology Affecting the Age of Diagnosis of Autism Spectrum Disorder. R. A. Mishaal*¹, E. Ben Itzhak² and D. A. Zachor³, (1)the autism center, assaf harofeh medical center, (2)Ariel University Center/ Assaf Harofeh Medical Center, (3)Tel Aviv University / Assaf Harofeh Medical Center

Background: Genetic and environmental factors have a role in the phenotypic expression of ASD. The signs of ASD usually appear prior to the age of 3 years, but typical symptoms were found as early as 6-12 months of age. Nonetheless, the diagnosis is commonly delayed. The factors that influence the age of diagnosis may be environmental, parental related and symptoms dependant. Early diagnosis and treatment of ASD improves the prognosis.

Objectives: The goal of this research was to identify children's characteristics that might delay the diagnosis of ASD and to increase the measures of survey in order to make an earlier diagnosis in this population. We focused on the correlation between the age of the diagnosis of ASD and parental experience, in terms of the child's birth order and whether the child had a former sibling diagnosed with ASD, as well as the parents' age and education. We also examined the influence of the severity of the autistic disorder's symptoms on the age of diagnosis.

Methods: The study was conducted at the Autism Center, a national tertiary center for diagnosis, treatment and research in the field of ASD. The cohort included 582 participants, 74 females and 508 males (F:M 1:6.9), aged 15 to 72 months (M=30.9m, SD=12.3m) at the time of diagnosis, all of whom received a diagnosis within the autistic spectrum. Assessment of ASD was obtained using standardized tests, the Autism Diagnosis Interview-Revised (ADI-R) and the Autism Diagnosis Observation Schedule (ADOS) and meeting criteria for autism/ASD based on DSM-IV criteria. Autism severity was assessed by using the new ADOS severity scale. Assessment of adaptive skills was made using the Vineland Adaptive Behavior Scales. Medical, developmental and familial histories were obtained from the parents, including data on child's gender, age, familial history and parental ages and education.

Data was collected between February 2002 and March 2012.

Results: A significantly higher rate of non-first-born children ($p < 0.05$) and a significantly higher rate of children with an older sibling with ASD ($p < 0.05$) was found among children diagnosed earlier with ASD, comparing to the later diagnosed children. Children with developmental regression were diagnosed with ASD significantly earlier than those without regression ($p < 0.01$). The lower the social and communicational functioning level was (by ADOS and ADI), the earlier the diagnosis was made ($p < 0.001$). Lower functioning level in adaptive skills domains (by Vineland) correlated with later diagnosis. No significant correlation was found between the child's gender, or paternal and/or maternal age or education and the age of diagnosis of ASD.

Conclusions: "Parental experience" (either being non-first-born child or a having an older sibling with ASD), a history of developmental regression and severity of ASD symptoms are all associated with an earlier diagnosis of ASD. Parents should be educated for early signs of ASD to prevent delay in diagnosis. Children who raise any suspicion of clinical signs of ASD should be referred to ASD specialist for extensive evaluation, since milder presentation may also delay the diagnosis.

106.063 63 Needs and Opportunities for ASD Awareness, Legislation, Intervention, Training and Research in Argentina. A. Rattazzi^{*1}, M. L. Massolo², K. A. Gutson¹, V. M. Ensenat³, C. Plebst¹, S. H. Cukier¹, M. Massolo¹, D. Melfi¹, N. Martinez¹, V. L. Martorello¹, P. Landolfi¹ and L. A. Croen², (1)*PANAACEA*, (2)*Kaiser Permanente Division of Research*, (3)*British Hospital of Buenos Aires*

Background: ASD knowledge and services in Argentina are limited and unevenly distributed throughout the country, with most resources concentrated in the main cities, such as Buenos Aires. Furthermore, there is a lack of coordination and communication between the various service providers, educators, parent advocacy organizations and government officials who are addressing the needs of the ASD community.

Objectives: To identify the major needs and opportunities throughout the country in the areas of 1) awareness and early detection, 2) legislation

and public policy, 3) intervention, and 4) training and research.

Methods: Information was gathered in two ways. First, an online survey was developed to be completed by parents, clinicians, educators, and individuals with ASD throughout the country. The survey solicited responses regarding two local needs and opportunities in each of the 4 themes mentioned above. Information about the respondent, including age, gender, city and province, and relationship to ASD, was also collected. The survey instrument was distributed broadly via social networks and also sent directly to individuals in the ASD community. Second, a stakeholder meeting was held in Buenos Aires which was attended in person by 80 individuals from different institutions and organizations, including parents, professionals and legislators. In addition, the meeting was streamed live in order to facilitate participation of people living in the interior of the country. Needs and opportunities were identified through group workshops and interdisciplinary group discussions.

Results: Within 10 days of posting the survey online, more than 250 completed surveys had been received from almost every province in the country. Detailed results from the survey and stakeholder meeting will be presented.

Conclusions: The participation of people from all disciplines and geographic areas in Argentina in the identification of needs and opportunities in relation to ASD awareness, legislation, intervention, training and research provides valuable qualitative information pertinent to local communities. This information is essential for the development of successful and sustainable ASD programs at the local and national levels.

106.064 64 Early Symptoms of Autistic Disorders in Korean Children: Retrospective Findings for 1- and 2-Year-Old Children. Y. Lee^{*1}, E. Lee¹ and H. Seung², (1)*Hallym university*, (2)*California State University*

Background: Generally, it has been recommended that the diagnosis of autistic disorders be reserved until age 3-4 years because the three core deficits of autistic disorders can be identified reliably after 3 years old (Bryson, 2007; Coonrod & Stone, 2005, Chawarska & Volkmar, 2005). However, many researchers have reported that early symptoms of autistic disorders could be

identified relatively early (Baranek, 1999; Werner et al., 2000; Maestro et al., 2001, 2002; Osterling, Dawson, & Munson, 2002). These early symptoms have been reported through parent's retrospective reports (Chawarska & Volkmar, 2005). Early identification is very important because it has the potential to improve intervention outcomes (Stone et al., 2000; Wetherby et al., 2004).

Objectives: This study aimed to compare the occurrence of early symptoms in Korean children among three groups (autism, intellectual disability, and typically developing children) through retrospective parent reports. We used a Korean translation of the First Year Inventory (Watson et al., 2007). Additionally, we aimed to compare the results with the findings in English speaking children.

Methods: Thirty parents who have children with (a) autistic disorders (AD; n=10), (b) intellectual disabilities (ID; n=10), and (c) normal development (ND; n=10) participated in the study. The groups were matched for chronological age. The children's age range was 3;0 through 8;10. Parents were asked to reflect on their children's behaviors when they were age one- and two-years while completing the FYI-retrospective version. The FYI includes eight constructs and is divided into two domains; social communication (social orienting and receptive communication, social affective engagement, imitation, expressive communication) and sensory-regulatory functions (sensory processing, regulatory patterns, reactivity, repetitive play & behavior). The total risk score and the risk points in the 2 domains and each of 8 constructs were calculated based on Reznick et al. (2007) and Watson et al. (2007).

Results: Data will be further analyzed using SPSS but preliminary results are reported herein. There were significant differences among the three groups in total risk score (1-year-olds, $F_{(2, 29)}=5.536$, $p<.05$; 2-year-olds, $F_{(2, 29)}=12.514$, $p<.001$) and risk points on social communication domains (1-year-olds, $F_{(2, 29)}=6.175$, $p<.01$; 2-year-olds, $F_{(2, 29)}=12.685$, $p<.001$). However, there were no group differences in the risk point on sensory-regulatory domain at either age.

Conclusions: Results indicated that Korean children with autistic disorders could be

distinguished from children with normal development at 1 year of age. The parents reported early symptoms of autistic disorders in social communication but not in the sensory regulatory domain. And the symptoms became more salient at age 2 years. Results of the current study also indicate that the Korean version of the FYI could be used in screening developmental delay in children under two years old. Validation with a larger prospective sample is clearly indicated.

106.065 65 Maternal Exposure to Childhood Abuse Is Associated with Elevated Risk of Autism. A. L. Roberts¹, K. Lyall¹, J. Rich-Edwards², A. Ascherio¹ and M. G. Weisskopf^{*1}, (1)*Harvard School of Public Health*, (2)*Brigham and Women's Hospital*

Background: Adverse perinatal circumstances have been associated with increased risk of autism. Women exposed to childhood abuse experience more adverse perinatal circumstances than women unexposed, but whether childhood abuse is associated with autism in offspring is unknown.

Objectives: To determine whether maternal exposure to childhood abuse is associated with increased risk of autism, and whether possible increased risk is accounted for by higher prevalence of adverse perinatal circumstances among abused women.

Methods: We identified children with autism spectrum disorders (ASD) of mothers in the Nurses' Health Study II, which includes women from across the entire United States. Children with ASD were identified by maternal report (n=451), validated with the Autism Diagnostic Interview-Revised in a subsample. Controls (n=52,498) were children of women who did not report autism in offspring; a single child was randomly selected if a control mother had more than one child. Combined childhood physical and emotional abuse and sexual abuse was assessed via a questionnaire administered separately from the questionnaire about children with ASD. We used generalized estimating equations with a log link and Poisson distribution to estimate risk ratios and 95% confidence intervals (CI) for the association between exposure to childhood abuse and risk of autism in the children of mothers.

Results: Exposure to abuse was associated with increased risk of autism in children in a monotonically increasing fashion. The highest level of abuse was associated with the greatest prevalence of autism (1.8% versus 0.7% in women not abused, $P = 0.005$) and the greatest risk for autism after adjustment for demographic factors (risk ratio=3.7, 95% confidence interval=2.3, 5.8). All adverse perinatal circumstances were more prevalent in women abused except low birth weight. Adjusted for perinatal factors, the association of maternal abuse with autism was slightly attenuated (highest level of abuse, risk ratio = 3.0, 95% confidence interval=1.9, 4.9). In these models low birth weight (<5 pounds), gestational diabetes, smoking during pregnancy, abortion prior to birth, and intimate partner abuse in the calendar year before the birth year were all associated with higher risk of ASD, but toxemia, alcohol intake, and pregnancy duration were not.

Conclusions: We identify an intergenerational association between childhood exposure to abuse and risk for autism in the subsequent generation. Adverse perinatal circumstances accounted for only a small portion of this increased risk.

106.066 66 Age of Autism Diagnosis in a Clinical Setting: Differences by Rural Vs. Urban Counties. C. Hall*¹, M. Lambha² and J. Hamel², (1)*The Marcus Autism Center*, (2)*Marcus Autism Center*

Background: Early identification and accurate diagnosis of autism spectrum disorders is critical, since earlier exposure to intervention is associated with better outcomes. Unfortunately, access to specialists and early diagnosis can be limited for traditionally underserved populations (Liptak et al, 2008), and previous studies have shown later age of diagnosis associated with income level, geographic location (Mandell et al, 2005), and race/ethnicity (Valicenti-McDermott et al, 2012). The present study examines factors that may influence age of diagnosis in a clinical setting at the Marcus Autism Center; a center that serves a diverse geographic and socioeconomic population in the Atlanta metropolitan area.

Objectives: The purpose of this study is to analyze the age of first diagnosis in a clinic setting and the extent to which this age is influenced by factors including race/ethnicity, gender, type of insurance (medicaid vs. private insurance) and geographic

location (rural vs. urban). Autism spectrum subtype was also examined as a predictor of age of first diagnosis.

Methods: A record review was conducted of 343 diagnostic evaluations conducted between November 2010 and November 2011 at the Marcus Autism Center. To be included in this study, the evaluation had to include the following components: Diagnostic interview, a developmental/cognitive measure (e.g. Bayley Scales, DAS-II), an adaptive measure (e.g. Vineland Scales), and the Autism Diagnostic Observation Scale (ADOS). Information extracted from the records included child's age, race/ethnicity, gender, county of residence, insurance information, prior diagnosis, and primary diagnosis given after receiving the comprehensive assessment. The child's county was classified as rural or urban using rural-urban continuum codes developed by the United States Department of Agriculture (USDA). Of the 343 reports reviewed, 132 children received a first time diagnosis of autism spectrum disorder, and these were included in the following analyses.

Results: The average age of autism diagnosis in this clinical setting was 63 months. However, use of one-way ANOVA showed that the age of diagnosis differed significantly based on ASD subtype; $F(2, 129) = 9.01, p < .001$ (Autism = 56 months; PDD NOS = 69 months; Asperger's disorder = 89 months). There were no differences in age of diagnosis by race/ethnicity, gender, or insurance type (medicaid vs. private insurance/self pay). However, use of an independent samples t-test demonstrated that children who lived in rural counties had a significantly higher age of diagnosis of autistic disorder (70 months) compared to those children living in urban counties (52 months); $t(82) = 2.58, p < .05$. The age of diagnosis for children with PDD NOS and Asperger's disorder did not differ based on geographic location, as children in both categories had an older age of diagnosis in general.

Conclusions: These findings show an average age of first autism diagnosis of 5.8 years among children in rural counties, compared to 4.3 years for children living in urban counties. This large difference highlights the importance of efforts to increase outreach and education for providers in

rural counties, as well as efforts to improve access to information, specialists and diagnostic assessment for children living in these areas.

106.067 67 Children with Past but Not Current Diagnosis of Autism Spectrum Disorder. S. J. Blumberg*¹, R. M. Avila², L. J. Colpe³, B. Pringle³ and M. D. Kogan⁴, (1)*Centers for Disease Control and Prevention*, (2)*University of Washington*, (3)*National Institute of Mental Health*, (4)*Health Resources and Services Administration*

Background: The 2007 (U.S.) National Survey of Children's Health showed that approximately 1-in-100 children aged 3-17 years had autism spectrum disorder (ASD) based on parent report, and nearly as many children (approximately 1-in-150) had once been diagnosed with ASD but did not have the condition at the time of the interview. Understanding why parents might not have reported a current diagnosis for children with a past ASD diagnosis may be an important step toward better use of parent surveys to monitor ASD prevalence and the health care needs of this population.

Objectives: We evaluated whether children reported to have a past but not current diagnosis of ASD differed from children with a current diagnosis of ASD on sociodemographic characteristics, health care service use, diagnostic history, functional limitations, and present symptomatology.

Methods: The Survey of Pathways to Diagnosis and Services was a nationally representative telephone survey conducted by the (U.S.) Centers for Disease Control and Prevention's National Center for Health Statistics in 2011. The general purpose was to explore the health care and diagnostic history of school-aged (6-17 years) children with special health care needs (CSHCN) who were ever diagnosed with ASD, intellectual disability, and/or developmental delay. We completed 1,420 interviews with parents of CSHCN who reported that their children had a current diagnosis of ASD. In addition, we completed 187 interviews with parents of CSHCN who reported that their children had a past but not current diagnosis of ASD. In this presentation, we compare estimates for these two groups.

Results: CSHCN who have a past but not current diagnosis of ASD were less likely than CSHCN with current ASD to currently have difficulty asking for things they need/want (9% vs 22%) and getting around by biking, walking, driving, or public transportation (23% vs 52%). They also were less likely to currently receive school-based social skills training (22% vs 50%) and non-school-based services to meet their developmental needs (56% vs 70%). No statistically significant demographic differences were observed.

Approximately 4 in 5 CSHCN with a past but not current diagnosis of ASD have parents who believe that their child never had ASD, yet results from the Children's Social Behavior Questionnaire suggest that many of these children have elevated symptoms consistent with ongoing pervasive developmental delay.

Conclusions: Parents may have more difficulty answering survey questions about children's current developmental conditions when these children currently exhibit fewer limitations and require fewer services than they did at an earlier age.

106.068 68 Assessing Autism in Mexico Through the Autism Behavior Checklist (ABC). L. Albores-Gallo*¹, C. List Hilton², K. Living Varela Orozco³, O. Roldán-Ceballos⁴ and A. P. Maurer-Martínez⁵, (1)*Hospital Psiquiátrico Infantil "Dr. Juan N. Navarro" Secretaría de Salud*, (2)*Washington University School of Medicine, St. Louis, Missouri, USA*, (3)*Hospital Psiquiátrico Infantil "Dr. Juan N. Navarro" Secretaría de Salud*, (4)*Hospital General "Dr. Fernando Quiroz Gutiérrez"*, (5)*Iberoamericana University School of Psychology*

Background:

The alarming increase in the prevalence of autism spectrum disorders ASD (1 in every 80 in USA, 2006), makes early detection very important. Therefore, the use of easy screening methods, which do not require special training, with high reliability and sensitivity are needed. Even though Mexican versions of M-CHAT and SRS have been published, instruments oriented towards the educational settings are yet to be validated (Albores et al. 2011, Fombonne, 2011).

The Autism Screening Instrument for Educational Planning (ASIEP) developed by Krug et al. (1980), has five components which measure: behavior, vocalization, interaction, learning rate and

educational status. The Autism Behavior Checklist (ABC) is one of the five components of the ASIEP developed to assess symptoms in individuals with autism spectrum disorders (ASD) to be used in a school setting. The ABC provides different profiles for individuals from 18 months to 35 years of age may be answered by teachers or parents and does not require specialized training and has an adequate validity and reliability (Krug, Arick, & Almond, 1980).

Objectives:

To evaluate the validity and reliability of the ABC Spanish version.

Specific Objectives:

To evaluate the Spanish ABC :

- internal consistency (Cronbach alpha).
 - test- retest reliability.
 - convergent validity with the Autism Diagnostic Interview- Revised (ADI-R).
 - construct validity.

Methods:

Participants were 133 children (aged 2-17), with a presumptive diagnosis of autism. After translating and backtranslating the ABC all parents answered the checklist, the ADI-R and a semi-structured interview to confirm an ASD diagnosis.

The sample for the ABC test-retest analysis consisted of 19 parents with unaffected typically developing children between 2 and 17 years old.

Results:

A total of 133 children and adolescents with a mean age of 6.9 years (SD 3.7), age range of 2-17 years, 83.5% were males (n=111) and 16.5% were females (n=22). The ABC total mean score was 69.3 (SD 25). Males had the highest scores in all subscales. The Internal consistency was through the Cronbach Alfa coefficient which was: $\alpha = .83$ $p < .001$ for the 57 ABC items.

The 10 day test-retest reliability showed a Pearson correlation coefficient of $r = .98$, $p < 0.001$ and $r < = 1.00$., $p < 0.001$.

The Spearman correlation coefficients between the ABC subscales and the ADI-R ranged from ($r^s = .494$) to ($r^s = .816$).

Criterion validity with a cutoff of 30 resulted in a sensitivity of 87% and a specificity of 37%. The best Kappa was .285 between the ABC and the ADI-R.

Conclusions:

In this study we investigated the psychometric properties of the ABC Spanish adaptation version. As with other instruments the cutoff points proposed by the authors (Krug, Arick, & Almond, 1980) resulted in an underestimation of autism symptoms in women, leaving some females not classified as autistic.

Mexican parents show confusion when answering the checklist especially when a chosen item had a "high weight" that they thought did not reflect the "symptom severity." All difficulties were resolved by removing the assigned weight and asking them to rate each item in a true/false option.

106.069 69 The Influence of Self-Esteem in Predicting Changes in Autism Spectrum Behaviors for Adolescents with ASD: The UCLA PEERS School-Based Curriculum. R. Bagrodia*¹, D. Janulaitis¹, L. C. Tucci², Y. Bolourian³ and E. Laugeson⁴, (1)*The Help Group - UCLA Autism Research Alliance*, (2)*The Help Group/UCLA Autism Research Alliance*, (3)*UCLA PEERS Clinic*, (4)*UCLA Semel Institute for Neuroscience & Human Behavior*

Background:

In typically developing adolescents, high self-esteem or self-concept has been linked to peer acceptance and social activity (McDougall, Hymel, Vaillancourt, & Mercer 2011). This relationship has been seen to also exist for youth with Autism Spectrum Disorders (ASD; Atwood, 2003), who regularly face deficits in social behavior, and tend to suffer from self-blame, low self-esteem and peer rejection. The Program for the Education and Enrichment of Relational Skills (PEERS®) is a 14-week evidence-based social skills intervention that

addresses poor social skills for adolescents with ASD by teaching lessons on how to make and keep friends. Previous research indicates that PEERS® is effective in improving overall social skills for youth with ASD; however, the extent to which self-esteem predicts treatment outcome has yet to be investigated.

Objectives:

This study examines how youth-reported self-esteem predicts improvement in parent-reported autism spectrum behaviors related to social skills following a school-based, teacher facilitated social skills intervention for middle and high school adolescents with ASD.

Methods:

Participants included 146 adolescents, ranging from the age of 11-18 ($M=15.08$; $SD=1.82$). Participants received approximately 30 minute of daily social skills instruction over a 14-week period. Teachers provided instruction on the PEERS® curriculum through didactic presentation, role-play demonstrations, behavioral rehearsal activities, and review of socialization homework assignments. In order to understand the relationship between self-esteem and treatment outcome, students completed the Piers Harris Self-Concept Scale Second Edition (PHS2; Piers, Harris, and Herzberg, 2002) at post-test to measure self-esteem, while parents completed the Social Skills Improvement System (SSIS; Gresham and Elliott, 2008) at pre-test and post-test to evaluate social skills treatment outcome. Pearson correlations were calculated to examine the relationship between PHS2 subscales and the SSIS Autism Spectrum Subscale, which measures behaviors such as preoccupation with objects, perseveration, and poor eye contact.

Results:

Results revealed that higher youth-reported overall self-esteem on the PHS2 significantly predicted improvement in parent-reported autism spectrum behaviors on the SSIS ($p<.02$), particularly in the areas of Behavioral Adjustment ($p<.04$), Physical Appearance ($p<.03$) and Happiness ($p<.01$). Intellectual Status ($p<.07$) and Freedom from Anxiety ($p<.07$) on the PHS2

predicted treatment outcome on the SSIS Autism Spectrum subscale at trend levels. The PHS2 Popularity subscale did not predict improvement in autism spectrum behaviors on the SSIS.

Conclusions:

These findings suggest adolescents with ASD who report higher self-esteem are less likely to demonstrate autism spectrum behaviors related to social skills following treatment, according to parent report. In particular, adolescents receiving the PEERS® intervention in the classroom who endorse fewer problematic behaviors, greater confidence in personality attributes and physical appearance, and greater happiness and satisfaction post-treatment are more likely to decrease nonfunctional routines and rituals present in their daily lives.

106.070 70 Effect of Social and Environmental Factors On the Prevalence of Autism in Qatar. F. Alshaban*, *Shafallah Medical Genetics Center*

Background:

The symptoms of ASDs typically are present before age 3 years and often are

accompanied by abnormalities in cognitive functioning, learning, attention, and sensory

processing.

A formal diagnosis is generally not made until the age of five.

The vast majority of cases of autism are idiopathic, the best scientific evidence

available to us today points toward a potential for various combinations of factors,

namely multiple genetic components and certain environmental and socio-economic

factors. Timing of exposure during the child's development (before, during or after

birth) may also play a role in the development or final presentation of the disorder.

Objectives:

To estimate the effect of certain socio-economic and other risk factors on the

prevalence of Autism in Qatar.

Methods:

The target population for this study are children diagnosed with Autism attending the

Shafallah Center for children with special needs.

Clinical evaluation is conducted by a developmental psychologist, and/or pediatrician, it

includes a medical, developmental, and behavioral history; a standard physical and

neurologic examination, In addition, the Autism Diagnostic Interview (ADI-R), and

Autism Diagnostic Observation Schedule-G (ADOS-G) will be administered.

Results:

Preliminary analysis of 171 subjects showed the highest prevalence among age group

7-14 years (61%).

Male/female ratio was 82% /18%, which is around 5/1.

Other factors like consanguinity, education, and family income found to have an effect

on the prevalence of the disease in Qatar.

Conclusions:

Obtaining a reliable estimate is important in planning for providing the best health care

and educational services needed to improve the overall outcome of Autism in Qatar.

106.071 71 The “Prima-Pietra” Project: A Web-Based Platform for Early Autism Risk Assessment. L. Ruta*¹, R. Siracusanò², G. Tortorella², M. Boncoddò², C. Colombi³, G. Crifaci⁴, L. Billeci⁵, G. Tartarisco⁶, M. Ferro⁷, A. Narzisi⁸, F. Muratori⁸ and G. Pioggia⁹, (1)*Institute of clinical physiology, National Research Council*, (2)*Universita' di Messina*, (3)*National Research Council of Italy*, (4)*nstitute of clinical physiology, National Research Council*, (5)*Institute of Clinical Physiology, National Council of Research*, (6)*National Council of Research (CNR)*, (7)*“Antonio Zampolli” Institute for Computational Linguistics*, (8)*University of Pisa – Stella Maris Scientific Institute*, (9)*Institute of Clinical Physiology, National Research Council (CNR)*

Background:

It is well recognized that the best outcomes in autism spectrum disorders (ASD) are achieved through early diagnosis and early intervention. ASD symptoms may occur as early as 12-18 months and different instruments have been developed for early autism risk assessment under the age of 2 years. The Modified Checklist for Autism in Children (M-CHAT) is a developmental surveillance-screening instrument administered during 18- to 36-month well-child visits that was demonstrated to improve early identification of autism. Novel technologies can substantially contribute to improve early diagnosis in ASD, providing early screening risk assessment platforms, unobtrusive measurements of behaviors and physiological responses, as well as brain structure and connectivity, or other measurable stimulus-event experimental paradigms. The Prima Pietra Project based at the Pervasive Healthcare Center of the Institute of Clinical Physiology of the National Research Council of Italy (Consiglio Nazionale delle Ricerche, C.N.R.) and the AOU Polyclinic “G. Martino” in Messina developed and provided an early autism risk assessment web-based platform for pediatricians and physicians available on the internet.

Objectives:

The first aim was to exploit the Prima Pietra web-based platform for early remote autism risk assessment with Italian pediatricians in terms of accessibility, usability and acceptance of the system by the users in their clinical routine. The

second aim was to enhance the possibility for an early diagnosis in the metropolitan area of Messina applying the screening web-based platform.

Methods:

The Prima Pietra web-based screening platform is accessible by any web browser. The platform enables the user to add, retrieve, analyze, and mine personal, physiological and behavioral data interacting with a remote secure database management system. The platform allows the child's information and the M-CHAT scores to be entered by the pediatricians (who also administered the MCHAT to the parents in a face-to-face way) during the routine 18 - 36 months periodic health monitoring controls. If a child fails the checklist, the platform alerts via e-mail the Prima Pietra team and a trained psychologist administers a structured phone interview with the parents in order to verify the risk profile of the child. The platform has been applied for 9 months.

Results:

49 out of 108 (45%) pediatricians of the metropolitan area of Messina (Sicily) accepted to take part in the study and were trained to use the Prima Pietra web interface. The participants applied the platform to 483 children during 18- to 36-months well-child visits. 44 children were identified by the platform as failing the MCHAT checklist and were selected for the structured phone interview. An autism risk was assessed for 6 children out of 44 children.

Conclusions:

Our preliminary findings demonstrate that the design and implementation of a web-based surveillance system for early autism screening is well accepted by paediatricians and substantially supports early diagnosis in ASD enabling a promptly early intervention strategy.

106.072 72 Preliminary Data for the CAST Test in Three Spanish Population-Based Birth Cohorts At 5 Years of Age, in the INMA (INfancia y Medio Ambiente [Environment and Childhood]) Project. A. Aranbarri*¹, J. Forn², A. Andiarana³, J. Julvez², C. L. Rodríguez-Bernal⁴, M. Rebagliato⁴ and I. Hertz-Picciotto⁵,

(1)University of the Basque Country (UPV/EHU), (2)Centre for Research in Environmental Epidemiology (CREAL), (3)BioDonostia Health Research Institute, (4)Center for Public Health Research, (5)UC Davis M.I.N.D. Institute

Background: The Childhood Asperger Syndrome Test (CAST) is a 37-item parental self-completion questionnaire designed to screen high-functioning autism spectrum in children 4 to 11 years (Scott, Baron-Cohen, Bolton, & Brayne, 2002). In a population-based school age study established in UK, the authors found a significant gender difference, where boys had a higher CAST score (Mean 5; IQR: 3,8) than girls (Mean 4; IQR: 2,6) (p-value <0.001) (Williams et al., 2008). There are few population-based school age studies that have use CAST and to our knowledge only one in Spanish population, in Gipuzkoa (Fuentes et al.,IMFAR 2010).

Objectives: To describe the preliminary results of CAST in three Spanish population-based cohorts; including the relation of sociodemographic variables and the multivariable analysis of longitudinal cognitive and clinical test scores.

Methods: The INMA (INfancia y Medio Ambiente [Environment and Childhood]) Project (<http://www.proyectoinma.org/>) is a network of seven prospective population-based birth cohorts in Spain, which aims to study the role of environmental pollutants (air, water and diet) during pregnancy and childhood in relation to child growth and development. We used CAST Spanish translated version by Fuentes, J., and Pezzuto, C., retrieved in 2009, from http://www.autismresearchcentre.com/arc_testsin 412 children at 5 years old (Sabadell cohort). We also used Bayley Scales of Infant Development (BSID) at 14 months, and McCarthy Scales of Children Abilities (MSCA) at 5 years to assess global cognitive development. Finally, the diagnostic criteria of DSM-IV for Attention Deficit Hyperactivity Disorder (ADHD) were applied to evaluate the ADHD symptomatology.

Results: In our population, the CAST mean score was 5.16 (SD 3.07). We found significantly higher mean scores in males [5.68 (SD 3.48)] compared with females [4.6 (SD 2.45)] (p-value <0.001). The children of mothers of lower socioeconomic

class or mothers with lower education level had significantly higher CAST scores (higher symptomatology) than those children of mothers of higher socioeconomical class or university level education. In multivariate models, adjusted for child's sex, maternal social class and maternal education, children whose mothers scored higher in the global severity index of SCL-90-R, defined as worse maternal mental health score, were more likely to have higher CAST score [IRR 1.30; p-value=0.028]. According to the DSM-IV, children with higher score in the symptomatology of ADHD combined criteria, were more likely to have higher score at CAST [IRR 1.59; p-value=0.006]. We found 4 children who exceeded the clinical cut-off of CAST (0.97%), 3 of them were boys and had similar profile with low cognitive score at BSID at 14 month, high cognitive score at MSCA and high score in ADHD symptoms.

Conclusions: These preliminary results on the CAST show consistency with a previous population study in UK and Spain. The study offers the second Spanish population-based data in 5 year-old children for the CAST test, including sociodemographic and mental health factors, longitudinal cognitive development and co-morbidity with ADHD symptoms. Further data for two INMA cohorts will be available by December this year, adding the Gipuzkoa and Valencia Cohorts to these data (with an estimated total sample of 1200 children).

106.073 73 Prevalence of the Autism Phenotype in Children Adopted After Early Neglect and Maltreatment. J. Green*, C. Kay and K. Leadbitter, *University of Manchester*

Background: The finding that 6% of 111 children adopted into U.K. families from Romanian institutions following severe early social deprivation showed 'quasi-autistic' patterns of social impairment in early childhood, with a further 6% showing isolated autistic features (Rutter et al 1999), had significant impact in suggesting a possible environment-related aetiology for an autism phenotype. An important question has remained – with both theoretical and practical implications – as to whether such autistic-like impairments might also be found in children adopted after early severe maltreatment or neglect in countries not using institutional care.

Objectives: To make a systematic and rigorous investigation into the presence of the autism spectrum disorder (ASD) phenotype in children after maltreatment.

Methods: Fifty-nine domestically adopted children (mean age 102 months (SD 20); 47% male) were recruited via a UK national charity (Adoption-UK). Seventy-three percent had experienced severe maltreatment with a mean of 1.6 (SD 1.2) of different maltreatment categories (emotional, physical, sexual abuse and neglect). Mean age at admission to out-of-home care was 11 months (SD 15); mean age at adoption was 35 months (SD 27); mean number of previous placements was 2.5 (SD 1.8). **Initial screening** for ASD symptoms and other psychopathology used the Development and Wellbeing Assessment (DAWBA; Goodman et al 2000), a detailed online parent symptom report used in national UK (Meltzer et al, 2000) and other large-scale epidemiological studies (Green et al, 2005, Ford et al, 2007). The DAWBA uses symptom report plus expert clinician review (blind to study hypotheses) to generate algorithm probabilities for DSM-IV diagnostic criteria. Individuals screening positively for ASD on the DAWBA were invited to a **second phase detailed assessment** including: i) Autism Diagnostic Interview-Revised, Autism Diagnostic Observation Schedule; ii) clinical diagnostic assessment; iii) biometrics and rating of minor physical anomalies (associated with neurodevelopmental risk such as fetal alcohol syndrome); iv) interview data on birth family history of ASD, psychopathology, and substance or alcohol misuse in pregnancy.

Results: Screening data analysed to date on 54/59 children suggests a high prevalence of autistic symptomatology. Three (5%) meet DAWBA criteria for >70% probability of ASD diagnosis and a further twelve (22%) for possible ASD criteria (>3% probability). These 15 adoptees are being assessed in detail as above during the **second phase**. Three of the first 10 of these phase 2 cases show ASD, with a further 7 showing 'Broad ASD' (partial features) using the Collaborative Program of Excellence in Autism (CPEA) criteria (Lainhart et al. 2006).

Data available for the IMFAR presentation will include; i) Complete ADI-R, ADOS and clinical examination data for autism and 'quasi-autism'

symptoms; ii) complete maltreatment indices and data on physical phenotype, including evidence for fetal alcohol syndrome or other biological vulnerability; iii) birth family history.

Conclusions: This data will give to our knowledge the first rigorous data on the presence of ASD in a high-risk adoption sample from non-institutionalized care in a high-income country. It has potentially substantial theoretical and clinical implications.

Clinical Phenotype Program

107 Screening and Diagnosis

Moderators: L. Gallagher¹, L. Zwaigenbaum² (1)Trinity College Dublin, (2)University of Alberta

A range of factors impacting on diagnosis and screening will be highlighted in the abstracts presented in this session. The validity of many screening and diagnostic instruments are considered in a number of cultural contexts. Also considered are factors influencing diagnosis and screening including the impact of lifespan and other vulnerability factors.

107.075 75 Factors Influencing How Parents Report Autism Symptoms On the ADI-R. R. M. Jones*¹, D. M. Wexler¹, D. K. Anderson², S. Risi³, C. Corsello⁴ and C. Lord¹, (1)Weill Cornell Medical College, (2)University of Michigan, (3)Eastern Michigan University, (4)University of California, San Diego

Background: The Autism Diagnostic Interview (ADI-R) is often used for clinical and research diagnostic purposes.

Objectives: Many have hypothesized that caregivers exaggerate or understate autistic symptoms, based upon when in the child's life they are asked to remember behaviors. Two studies determined whether caregivers anchor their perception of prior symptoms based upon the current functioning of the child as described on the ADI-R.

Methods: In the first study, a between subjects design, three formats of the ADI-R were administered to randomly chosen samples of caregivers whose children were matched on age, IQ and ASD diagnosis. 32 caregivers reported current symptoms on the ADI-R for all questions and then reported prior history of symptoms. 30 caregivers reported prior history of symptoms for

all questions followed by current symptoms. 88 caregivers answered the ADI-R questions in the typical format, reporting current and prior history of behaviors together. Analyses were conducted comparing the two groups who received the ADI questions separated by time on algorithm totals for current and past behaviors and secondary analyses compared the three groups. In the second study, a within subjects design, data on the ADI-R was collected from 102 caregivers of children with suspected ASD or non-spectrum delay at 5 and 9 years of age. Analyses were conducted comparing how caregivers reported symptoms when the child was 4 -5 versus how caregivers reported symptoms about this same time period retrospectively when the child was 9 years of age.

Results: In the first study, caregivers who were first asked only current questions had higher totals for both current and prior history of symptoms compared to caregivers who were first asked only previous history of behaviors. Caregivers who were first asked only previous history of symptoms had lower totals of prior behaviors compared to caregivers who were first asked current behaviors and to those who were given the ADI-R in a typical format. In the second study, caregivers of children at age 9 retrospectively described their child's symptoms from age 5 as more severe compared to when caregivers were reporting the current symptoms at age 5. Caregivers retrospectively described more severe behavior problems at age 5 in children who had more internalizing or externalizing behaviors on the Child Behavior Checklist at age 9.

Conclusions: Overall these findings highlight the importance of using both current and prior history symptom questions on the ADI-R and that the current functioning of a child should be considered when using this instrument as a diagnostic tool. How parents report symptoms is complicated and it is crucial to consider the influence of both prior and current symptoms from caregiver reports in diagnoses.

107.076 76 Predicting DSM-5 ASD Diagnosis Using the Autism Mental Status Exam in an Adult Sample. D. Grodberg*¹, P. M. Weinger², D. B. Halpern¹, A. Kolevzon¹ and J. D. Buxbaum¹, (1)Mount Sinai School of Medicine, (2)Yeshiva University

Background: The assessment and diagnosis of Autism Spectrum Disorder (ASD) in adults is unreliable due to the absence of a brief observational tool that is validated to the gold standard ASD diagnostic assessment. The wider recognition of ASD in adults reflects clinicians' increased knowledge as well as a growing availability of evidence-based treatments and research protocols. Yet the diagnosis can be challenging in this underserved and under-studied population. The Autism Mental Status Exam (AMSE) was developed to address the lack of standardized observational assessment for ASD in non-academic settings. The AMSE is an 8-item diagnostic observational tool that structures the way we observe and record social, communicative and behavioral functioning in people with ASD. Each item is scored on a 0 to 2 scale yielding total scores that range from 0 to 16. Initial validation indicates that the AMSE has excellent inter-rater reliability and classification accuracy when compared to the Autism Diagnostic Observation Schedule (ADOS).

Objectives: To determine sensitivity and specificity of AMSE cutoff scores in predicting independent diagnosis of ASD using proposed DSM-5 criteria.

Methods: Forty consecutive subjects age 18-44 received comprehensive diagnostic testing as part of the assessment protocol at the Seaver Autism Center at Mount Sinai School of Medicine. All subjects were referred for suspected ASD. Each subject first received a clinical evaluation by a psychiatrist with expertise in ASD diagnosis during which the AMSE was administered. The subject was then administered an ADOS in a different exam room by a site reliable psychologist who was blind to the AMSE score or the psychiatrist's diagnostic impressions. When feasible, an ADI-R was also administered. Best Estimate Clinical Diagnosis (BECD) was then ascertained by a psychologist at the center who is research reliable on the ADOS. BECD protocol involved communication with the ADOS and ADI-R examiners. The BECD clinician remained blind to the psychiatrists' AMSE scores but was provided clinical notes that were limited to review of symptom domains, current medications, and medical history. The proposed DSM-5 criteria were then used to guide the BECD clinician's diagnostic formulation of ASD vs. non-ASD.

Results: Within this high-risk sample, 52.8% of participants met criteria for a diagnosis of Autism Spectrum Disorder based on research diagnostic instruments (ADOS, ADI) and proposed DSM-5 criteria. Diagnostic accuracy was assessed by the nonparametric measure of area under an ROC curve. The ROC curve analysis was used to determine a criterion cut-off score based on AMSE total scores. Area under the ROC curve was 0.99 (95% confidence interval [CI]: 0.96– 1.0). This indicates that the AMSE was able to differentiate between ASD and non-ASD diagnoses. The most effective cut-off score was estimated at a total score of greater than or equal to 5. This cut-off score produced a sensitivity of 100% and a specificity of 95% in this high-risk population. Total AMSE scores for non-ASD participants ranged from 0 to 5 and total AMSE scores for ASD participants ranged from 5 to 8.

Conclusions: The AMSE holds promise as a brief diagnostic observational assessment for ASD.

107.078 78 Is Serum Brain Derived Neurotrophic Factor (BDNF) a Reliable Biological Marker for Autism?. L. Hewitson*, T. Mauldin, A. Potts and C. Schutte, *The Johnson Center for Child Health and Development*

Background: Brain-derived neurotrophic factor (BDNF) plays an important role during neuronal differentiation and survival, and in the formation and plasticity of synaptic connections. Since disruptions in synaptic plasticity has been linked to autism, several studies have examined serum BDNF levels in children with autism but the results are conflicting. This may be due in part to a lack of diagnostic stringency, age of subjects, and/or different inclusion/exclusion criteria used in those studies.

Objectives: The objective of this study was to compare levels of BDNF in serum from well-characterized male and female children with and without autism to determine whether BDNF is a robust biological marker for ASD.

Methods: Twenty-one children with autism met the inclusion criteria for this study. An autism diagnosis was assessed by a licensed psychologist using the ADOS and ADI-R. Subjects in the ASD groups were not taking any medications for at least 2 weeks prior to participation in this study. Twenty-one age- and gender-matched healthy children, without siblings on the autism spectrum,

were included as controls. All controls completed a health history questionnaire and underwent a developmental screening using the ABAS-II. The mean age, standard deviation and age range for each study group are reported in Table 1. A fasting morning blood sample was obtained from all subjects, processed according to standard protocols and the sera frozen immediately at -80°C until use. Serum BDNF was measured by ELISA (R&D Systems) at the University of Maryland Cytokine Core Laboratory. Samples were diluted 1:20 and run in duplicate. BDNF data were reported as pg/ml serum. Linear regression was used for all analyses. Binary independent variables (i.e. ASD and gender) were dummy-coded and continuous variables (i.e. age) were mean centered prior to analyses.

Table 1: The mean age, SD and age range for subjects in each study group.

| Group | N | Mean Age (St Dev) | Range |
|-----------------|----|-------------------|---------|
| Males w/ ASD | 10 | 4.50 (1.57) | 2.3-6.6 |
| Females w/ASD | 11 | 5.21 (1.37) | 3.0-7.3 |
| Control males | 10 | 4.87 (1.20) | 3.1-6.3 |
| Control females | 11 | 5.14 (1.36) | 2.3-6.7 |

Results: Mean serum BDNF levels within each group is shown in Table 2. Overall, serum BDNF levels were lower in ASD subjects compared with controls ($t=-2.7$, $p=0.011$), however, there was no interaction between age or gender ($t=1.4$, $p=0.168$ and $t=-0.3$ and $p=0.770$, respectively).

Table 2: The mean +/- SEM levels of serum BDNF per group.

| Group | Mean BDNF (pg/ml) | SEM |
|---------------|-------------------|--------|
| Males w/ ASD | 676.42 | 88.44 |
| Females w/ASD | 788.31 | 114.53 |
| Control males | 1103.68 | 129.81 |

| | | |
|-----------------|--------|--------|
| Control females | 950.20 | 105.00 |
|-----------------|--------|--------|

Conclusions: These results suggest that serum BDNF is lower in children with autism compared to controls but there was no effect of age and gender. Serum BDNF may be a useful sub-diagnostic biological marker in ASD but further research is needed in a larger cohort to confirm this finding.

107.079 79 The Challenge of Making a Diagnosis:

Understanding the Diagnostic Variation Among Autism Professionals. C. A. Cowan*¹, L. V. Ibanez², E. Myers³ and W. L. Stone³, (1)Seattle Children's Hospital Autism Center, (2)University of Washington Autism Center, (3)University of Washington

Background: Diagnosis of children with Autism Spectrum Disorders (ASDs) is challenging for children who present confusing or conflicting symptoms. Providers of different professional disciplines often disagree regarding a diagnosis based perhaps on discipline perspective, opportunity for multi-disciplinary assessments, clinical experience and other variables. The current study investigates some of the factors that might relate to diagnostic challenges and disagreement by examining data collected from clinicians during an interactive, conference of diverse professional backgrounds in Washington State.

Objectives:

1. To describe and to evaluate the degree of diagnostic agreement for ASDs among and between participants of various professional disciplines as well as professional characteristics such as work setting and years of clinical experience.
2. To determine which professional characteristics and/or clinical observations are associated with assignment of an ASD diagnosis.

Methods: The conference attendees included medical providers, psychologists, speech language pathologists, and others ($n= 77$). Three cases were presented to the conference participants, including a 3 y/o boy, a 6 y/o girl and a 16 y/o boy. Each case was presented to attendees in sections, the first being historical information,

followed by viewing 30 minutes of edited ADOS testing and finally additional test information that was gathered after ADOS testing. Each participant was asked at the end of each section to complete a short questionnaire to evaluate their immediate diagnostic impressions. The online questionnaire data were collected simultaneously from each attendee using a web-based survey tool. Attendees were asked not to discuss their impressions until after entering their final conclusions, and then encouraged to discuss cases in small groups at the termination of each case presentation. We provide a frequency analysis of assignment of an ASD diagnosis by case for each professional discipline and characteristic. We will also query which characteristics are positively and negatively associated with the assignment of an ASD to a given case.

Results: For cases 1, 2, and 3 the percentage of medical providers who assigned an ASD diagnosis was 37.5%, 33.3%, and 64.7% respectively. Among the psychologists, the percentage of providers who assigned an ASD diagnosis was 23.8%, 50%, and 66.7% for the same cases. For each of the 3 cases, chi-square analyses indicated that psychologists were not significantly more likely to assign an ASD diagnosis than medical providers. The analysis is still ongoing, and we hope to provide a model of the associations of different professional characteristics or patient characteristics with assignment of an ASD diagnosis.

Conclusions: In our initial analysis, we have found that there is a lack of consistency among professional disciplines in assignment of an ASD diagnosis not necessarily attributable to differences in the diagnosticians' professional disciplines. To increase diagnostic consistency among the varied professionals who care for individuals with ASDs, more research should further characterize the varying diagnostic approaches between different professional disciplines. Our research will begin to address these approaches which could perhaps lead to more consistent identification and classification of this complex disorder.

107.080 80 Diagnosing Autism Spectrum Disorder: Who Will Get a DSM-5 Diagnosis?. R. G. Kent^{*1}, S. J. Carrington², A. S. Le Couteur³, J. Gould⁴, L. Wing⁴, J.

P. W. Maljaars⁵, I. Noens⁵, I. A. van Berckelaer-Onnes⁶ and S. R. Leekam¹, (1)Cardiff University, (2)Wales Autism Research Centre, (3)Newcastle University, (4)National Autistic Society, (5)University of Leuven (KU Leuven), (6)Leiden University

Background: Introduction of proposed criteria for DSM-5 Autism Spectrum Disorder (ASD) has led to concern that some high functioning individuals who currently meet diagnostic criteria for Pervasive Developmental Disorder (DSM-IV-TR/ICD-10) will not qualify for a diagnosis under the proposed changes.

Objectives: The aim of the study was to investigate who would meet criteria for a draft DSM-5 diagnosis in data that was not collected specifically for the purpose of diagnosis according to DSM-IV-TR or ICD-10.

Methods: To investigate this, a new DSM-5 ASD algorithm was designed and tested using the Diagnostic Interview for Social and Communication Disorders (DISCO). First, sensitivity and specificity was tested using a clinically-matched sample [$N=82$] and further tested using an independent dataset [$N=115$]. Second, the output of the DISCO DSM-5 algorithm was compared with that of the DISCO ICD-10 algorithm using a dataset of individuals ranging in ability and age ($N=200$). This included a subset with Gillberg's Asperger Syndrome (Gillberg et al., 2001) and a subset with ICD-10 Atypical Autism. Finally, modifications were made to the DSM-5 algorithm to improve sensitivity.

Results: Sensitivity and specificity was good for identification of cases with clinical autism (AUC $<.87-.89$ for the validation sample). Convergence was high between DISCO outputs for DSM-5 ASD and ICD-10 Childhood Autism (96%) and between DSM-5 ASD and Gillberg's Asperger Syndrome (90%). No age or gender effects were found. Across all samples, 13%, mostly high functioning, did not meet DSM-5 criteria. Removing the age of onset criterion increased sensitivity without reducing specificity. Adjusting the social communication criterion increased sensitivity but with loss of specificity.

Conclusions: Use of the DISCO DSM-5 algorithm indicates that the proposed DSM-5 changes should identify the majority of individuals who

currently receive a diagnosis of ICD-10 Childhood Autism or Gillberg's Asperger Syndrome.

107.081 81 Symptomatic Presentation of Autism in Toddlers: What Can We See in 10 Minutes?. T. P. Gabrielsen*¹, M. E. Villalobos², M. Farley³, L. A. Speer⁴, C. N. Baker⁵, J. Viskochil⁶ and J. Miller¹, (1)*Center for Autism Research*, (2)*Children's Hospital of Philadelphia*, (3)*University of Utah*, (4)*Cleveland Clinic*, (5)*Tulane University*, (6)*Utah Autism Research Program*

Background:

There have been recent emphases on ASD screening in health care settings and efforts to simplify identification of early signs of ASD. The structure of a typical health care appointment, however, may not elicit an accurate sample of a child's usual social behavior. Individuals with autism spectrum disorders (ASD) can exhibit grossly appropriate social behaviors some of the time. This may make it difficult for a clinician with limited autism expertise to detect subtle signs of ASD at very early ages by observation alone, which affects diagnostic impressions and subsequent referrals, and in turn can delay treatment during critical developmental periods. In the United States, typical primary care patient contact time is 10-20 minutes, which may not be sufficient observation time to form an accurate clinical impression of need for referral.

Objectives:

This study aimed to characterize differences in symptom presentation during brief clinical observations among children with and without ASD.

Methods:

Participants included 3 groups of children between the ages of 15-33 months: (1) children with early signs of ASD, (2) children with suspected language delay, and (3) typically developing children. Participants were from a large community pediatric practice in which 80% of all children presenting for care were screened with standardized tools for early signs of ASD. Only three children in the sample had previously been referred for an ASD evaluation and none were from high risk families. Families spoke

English or Spanish and had private insurance, Medicaid/CHIP, or were self-insured. Participants likely represented an ecologically valid sample of community families. A clinical evaluation for early signs of ASD (including the Autism Diagnostic Observation Schedule [ADOS]) was videotaped.

Social and communicative behaviors (e.g., initiating, responding, response to name, play and sounds) displayed by the children were measured across the first 10 minutes of the evaluation, and again 30 minutes into the evaluation for 10 minutes. Frequencies of grossly atypical and typical behaviors were compared among the 3 groups. Coders were licensed psychologists with ASD expertise who were research reliable on the ADOS and blinded to diagnostic group membership and screening results.

Results:

Findings suggest very young children with ASD can show grossly typical behavior much of the time, and that some children with ASD may not manifest significant atypical behavior within a 10-minute observation window. The ASD group showed statistically higher rates of atypical behavior and lower cognitive development and adaptive behaviors on standardized measures, but expert clinical impressions based on 10-minute observations were incorrect for children in the ASD group 39% of the time (false negatives). Clinical impressions were incorrect 25% of the time for children in the suspected speech delay group and 11% of the time for typically developing children (false positives).

Conclusions:

Brief observations likely do not provide enough of a behavioral sample to make a correct referral in all cases. Standardized screening tools identified more children as needing referral for ASD evaluation than clinical impression alone.

107.082 82 Distinguishing Autism Spectrum Disorders From Other Developmental Delays Using Blood Rnaseq. S. Letovsky*¹, M. E. Causey¹, M. Aryee², J. Skoletsky¹, C. Proulx¹, F. R. Sharp³, I. N. Pessah⁴, R. Hansen⁵, J. Gregg⁶ and I. Hertz-Picciotto⁷, (1)*SynapDx Corp*, (2)*Massachusetts General Hospital*, (3)*University of California Davis Medical Center; MIND Institute*, (4)*UC Davis M.I.N.D. Institute*, (5)*University of*

California, Davis, (6)MIND Institute, (7)University of California at Davis

Background:

There is an unmet need for objective biomarkers to assist clinicians in the early diagnosis of childhood neurodevelopmental disorders. A number of investigators have reported changes in blood gene expression associated with autism spectrum disorders; Voineagu reviews this literature, while Glatt et al describe a microarray blood gene expression classification signature for distinguishing children with autism spectrum disorders from typically developing children.

Objectives:

The aim of this study was to assess whether blood gene expression measured using next generation RNA sequencing (RNASeq) could provide a biomarker to distinguish children on the autism spectrum from children with other conditions that might present in the same clinical setting.

Methods:

The CHARGE (CHildhood Autism Risks from Genetics and the Environment) study recruited children between the ages of 2 and 5, some of whom were diagnosed on the autism spectrum, and others with other developmental delays. Subjects were grouped based on thresholds of the ADOS, ADI-R, Vineland and Mullens test into autism spectrum disorder (ASD) and other developmental delay (DD) groups to approximate the clinical use case of a secondary screen for autism in children suspected of neurodevelopmental disorders.

Blood samples were acquired from each subject in RNA-stabilizing PAXgene tubes. RNA was isolated and processed using the TrueSeq sequencing prep with poly-A selection for mRNA. RNASeq was then performed on an Illumina HiSeq 2000 Sequencer using 1/3 lane per sample. 174 ASD and 96 DD samples passed final QC, for a total of 270 samples.

Sequence data were processed through the Tuxedo RNASeq pipeline to yield counts per gene, which were normalized by downsampling. The

sample was divided into a training set (n= 153) and a holdout set (N=117), each of which was repeatedly randomly subsampled to achieve gender and age balance between the ASD and DD groups. On each iteration, informative features were selected by t-test and a support vector machine classifier was trained on a balanced subsample of the training set and tested on a balanced subsample of the holdout set; AUC's (area under the ROC curve) were averaged across iterations.

Results:

The mean AUC for the holdout set was 65.6 +/- 2.9%. When a 90% sensitivity threshold was selected on the classifier risk score, the mean specificity was 25.3, with 95% CI [13.6, 40.6%]. Gene categories found significant by ranksum test on the t-statistic include RNA processing, cell cycle, immune and inflammation-related GO categories.

Conclusions:

To our knowledge this represents the first report of a classification signature for ASD vs. DD using blood RNASeq. While the understanding of genetic contributions to autism spectrum disorders has been making impressive progress in recent years, genetic causes are individually rare, and are thus not sensitive in a diagnostic context. A gene expression signature with moderate AUC has potential clinical utility as a sensitive assay for identifying children at risk for ASDs within a population that is already suspected of neurodevelopmental disorders. Planned followup studies include a multicenter clinical study to further refine and validate a blood-based assay.

107.083 83 "Level of Support" in DSM-5: Untangling the Relations Between Adaptive Behavior, Cognitive Skills, and Autism Severity Scores in Seeking to Assign a Diagnostic Severity Level. A. S. Weitlauf*, A. Vehorn, K. Gotham, C. R. Newsom and Z. Warren, *Vanderbilt University*

Background: Proposed DSM-5 revisions to the diagnosis of Autism Spectrum Disorder (ASD) include a "severity" marker based on degree impairment in the domains of social communication and restricted and repetitive behaviors. Although qualitative differences

between Level 1 ("Requiring support"), Level 2 ("Requiring substantial support"), and Level 3 ("Requiring very substantial support") are described, quantitative methods or practice recommendations for differentiating between these levels have yet to be determined. This leaves the field vulnerable to discrepancies between severity categorizations reminiscent of current discrepancies between diagnostic categories (such as Asperger's, Autism, and PDD-NOS) which originally contributed to the push for a revised diagnostic schema. It is also unclear how these severity differentiations may change according to age and developmental level.

Objectives: To determine how severity estimates vary depending on age, cognitive skills, and adaptive scores in a large sample of children diagnosed with autism

Methods: Participants included 726 participants diagnosed with ASD, ages 15 months through 17 years, drawn from a university based clinical research database. Examined measures included the Vineland Adaptive Behavior Scales – II (Adaptive Behavior Composite, Communication, and Socialization scores), Autism Diagnostic Observation Schedule Comparison Scores (CS; also known as Calibrated Severity Score; Gotham et al., 2009) and several different measures of cognitive ability, including the Mullen Scales of Early Learning and Differential Ability Scales-II. Mild/No Impairment, Moderate, and Severe Impairment groupings were created in two ways. First, standard deviation splits were created by splitting data by standard deviation cutoffs (<70, 70-85, >85) for each measure. Next, tertile splits were created by separating the sample's scores into equivalent thirds for each measure. Grouping labels were compared for consistency across the three measures used to define level of impairment.

Results: Discrepancies emerged between all groups such that participants with Mild, Moderate, and Severe CS demonstrated varying levels of adaptive, communicative, social, and cognitive impairment. A large proportion of the Mild CS group fell into Moderate-to-Severe groups on Vineland and Cognitive variables (52%-85% based on standard deviation splits, 59-84% based on tertile splits). Many participants in the Mild/No Impairment IQ group were also defined as

Moderate-to-Severe based on the CS and Vineland variables (51%-90% for standard deviation, 35-72% for tertile). Discrepancies in severity classification for all variables were observed between standard deviation and tertile groupings as well as between age groups.

Conclusions: Discrepancies were found in the distribution of severity categorizations across adaptive, communicative, social, and cognitive functioning. Greater variability emerged when using tertile splits, suggesting that basing severity categorizations on comparisons with other diagnosed individuals within a group may lead to provider or site-specific biases in severity assessment. The differences between groups and age levels highlight the need for a more clearly elucidated method of classifying ASD diagnoses as mild, moderate, or severe according to proposed diagnostic labels, and further study of how those designations may change with development.

107.084 84 Determining the Efficacy of the SACS in Identifying Preschoolers with ASDs: Development of the SACS-Preschool (SACS-Pr). J. Barbaro*, E. Ulusoy and C. Dissanayake, *La Trobe University*

Background: The Social Attention and Communication Study (SACS; Barbaro & Dissanayake, 2010) adopted a developmental surveillance framework for the prospective identification of Autism Spectrum Disorders (ASDs) in infants and toddlers. This involved repeated monitoring of the early markers of ASDs at children's 12-, 18-, and 24-month routine health check-ups in a community-based setting. A follow-up diagnostic assessment was conducted at 48-months. Although the overall psychometric properties of the SACS were excellent, not all children later diagnosed with ASDs were identified as 'at risk' by 24-months. Thus, an additional SACS assessment during the preschool period may prove useful in the identification of children with ASDs who are not identified by 24-months.

Objectives: The aim in the current study was to: 1) develop a preschool version of the SACS to be added to the existing SACS framework; and to 2) identify the most predictive behavioural markers of ASDs on the SACS-Pr, which can effectively discriminate between preschoolers with and without ASDs.

Methods: The SACS-Preschool (SACS-Pr) was developed based on the original 24-month SACS checklist, and contains 22 behavioural items modified to reflect the developmental milestones of preschool aged children. An additional section, Repetitive, Stereotyped and Sensory Behaviours/Interests (RSSBIs), was added to reflect the emergence of these behaviours in the preschool period. A coder, blind to diagnostic status, observed video footage of the SACS follow-up assessments at 48-months ($n = 77$) and completed the SACS-Pr checklist for each child. Inter-rater reliability for each individual item, and the total checklist, was excellent. Follow-up assessments included administration of the Autism Diagnostic Observation Schedule and the Mullen Scales of Early Learning to 53 preschoolers with ASDs (Mean Age = 49.7 months), and 24 with Developmental and/or Language Delay (Mean Age = 47.1 months).

Results: Consistent with the original SACS results, the current study found that *Eye Contact*, *Pointing* and *Showing* continue to be key markers for the identification of ASDs in preschoolers. Additionally, *Social Smile*, *Follows Two Unrelated Commands*, *Reciprocal Social Interaction* and *Odd/Unusual Speech* were also identified as key markers of ASDs. Logistic regression analyses revealed that the best group of predictors for a diagnostic classification of ASD contained all of these key markers, with the omission of *Social Smile* and the addition of *Pretend Play*. Follow-up Receiver-Operating-Characteristic (ROC) analyses showed that this model, containing all eight variables, effectively discriminated between children with and without ASDs, with an excellent Area-Under-the-Curve value of 0.95.

Conclusions: The SACS-Pr was found to effectively discriminate between preschoolers with and without ASDs, in a referred sample. The behavioural items *Eye Contact*, *Pointing*, and *Showing*, found to be key markers of ASDs in infants and toddlers in the original SACS, continue to be key markers in preschoolers with ASDs, reinforcing the importance of repeated monitoring of these critical joint attention behaviours. The use of the SACS-Pr, alongside the original SACS, is currently being trialled in a community-based setting to determine its usefulness in the identification of preschoolers with ASDs in a low-risk sample.

107.085 85 Recent Advances in the Identification of Early Signs of Autism in First Year of Life Clinical Aspects Research. H. A. Alonim*, *The Mifne Center*

Background: Most recent research findings indicate that genetic and neurological factors associated with environmental aspects influence the phenomenon onset of autism. One of the assumptions is that as the population grows, new mutations emerge in the human genome, adhering to the polymorphs of the chromosomes A or B and contributing to the development of the autistic syndrome. It is still not possible to isolate and distinguish genetic, environmental and neuro-developmental factors. Many parents report; "Until the age of one year old my child developed properly and then there was a regression." What happens at that significant cutoff point between the first and second years of life? Does the clinical picture really change?

Objectives: In most western cultures children are diagnosed at a relatively early age (2-3) but even this age may be too late. It is advantageous to diagnose and treat early signs of autism during infancy because the brain develops dynamically at this early stage. The most accelerated neuron growth occurs in the first 18 months of life, creating a complex texture of cells that control the baby's sensory-emotional-cognitive regulation. A study conducted over the last decade examined 110 babies diagnosed with autism at the age of 2-3 years, using retrospective analysis of parents' video-recordings of their first year of life, (filmed before any suspicion concerning defective development arose).

Methods: The videotapes had recorded the babies from birth, from the age of several days or weeks at a high frequency that naturally differed from family to family worldwide. In addition to the videos collection, questionnaires were distributed to the parents. Variables investigated were: passivity, activity, eye contact, reaction to parents' presence, eating, reaction to touch, motor development and head circumference. All variables were measured blindly according to a validated evaluation form.

Results: Four categories emerged from analysis of the parents' responses : Group A: in 29.9% of the cases parents had suspected that something was inappropriate in their child's development.

Group B: in 22.4% of the cases, extended family members said that they felt something was wrong but did not tell the parents. Group C: in 8.4% of the cases family members had suggested the baby should be examined, but the suggestion was rejected by the parents. Group D: in 39.3% of the cases parents had not noticed any unusual signs. In the video-records analysis it was possible to identify early signs associated with autism characteristics in 98 of the 110 babies. Findings for 6 of the babies also showed pathological indices.

Conclusions: Findings from this study indicate that 89% of the studied babies originating from different cultures, already exhibited suspicious signs during the first 15 months of life. These findings (a) affirm the assumption that symptoms frequently appear in first year of life (b) indicate the urgent need to develop tools to identify risk for autism in first year of life. Such screening scale has been recently developed.

107.086 86 Parental Perceptions On the Diagnostic Process for Autism and Interest in A Genetic Risk Assessment Test for Autism Spectrum Disorders: An International Survey. C. Amiet^{*1}, V. Narcisa², M. Discenza³, E. Vaccari³, B. Rosen-Sheidley⁴, K. Carr⁵ and E. Couchon⁶, (1)*Groupe Hospitalier Pitié-Salpêtrière, APHP*, (2)*Acadia University*, (3)*Boston University School of Medicine*, (4)*Brandeis University*, (5)*University of Notre Dame*, (6)*IntegraGen Inc*

Background:

Autism spectrum disorders (ASD) are among the most common forms of developmental disability with a prevalence of 1 in 88 children and a sibling recurrence risk estimated at 18.7%. While multiple studies have shown that early intervention leads to a significantly improved long-term outcome, a significant time lag remains between the age when a difference in development is first suspected and the age of ASD diagnosis. Numerous studies have shown that ASD has a strong genetic component; however genetic tests currently available are primarily used for etiologic diagnostic purposes. Recent data provide evidence toward utility of a newly developed genetic risk tool to identify children with an increased risk of ASD among siblings of affected patients.

Objectives:

Our objectives were to: (1) understand parental experience with the ASD diagnosis process for their children, (2) obtain parental opinion regarding the potential use of a genetic risk assessment test for ASD.

Methods:

A self-administered survey was conducted using an internet-based questionnaire. Two versions of the survey were conducted consecutively. The first was an English language survey limited to U.S. residents who were parents or guardians of one or more children with ASD. The second survey was a French language survey for parents or guardians from France or other French speaking countries with one or more children with ASD. Responses to the U.S. survey were obtained between February 2012 and March 2012. The French survey was conducted from June 2012 to July 2012.

Results:

A total of 156 participants completed the U.S. survey and 554 participants (464 from France, 40 from Canada and 41 from other countries) completed the French survey. The mean time from a suspected difference in development to an ASD diagnosis was 22 months in the U.S. survey and 29 months in the French survey ($p < 10^{-4}$). The mean age of diagnosis was 57 months for both surveys. In each case, parents indicated delay in diagnosis was primarily due to a "wait and see" approach by the child's pediatrician or a delay in seeing a specialist.

In both surveys, the majority of parents (69%) indicated they would have pursued testing if a genetic test had been available which could determine if their child was at increased risk of developing an ASD. Similarly, 69% of parents from the French survey (n=106) and 80% of parents from the U.S. survey (n=25) with a younger undiagnosed child under 48 months of age indicated that they would want their younger child tested if a genetic risk assessment test were available, even if it could not confirm the diagnosis. Parents cited earlier access to evaluation and intervention, closer monitoring, and lessening of anxiety as reasons for wanting their child/children tested.

Conclusions:

Delayed diagnosis of ASD remains an issue even when a child is suspected of having a difference in development at an early age. The results of this survey indicate that the majority of parents would have been interested in a genetic risk assessment test for their younger children.

107.087 87 Use of the Development and Well-Being Assessment (DAWBA) to Identify Autism Spectrum Disorder in a Community Sample of Adolescents. F. S. McEwen^{*1}, C. Ames¹, E. L. Woodhouse¹, E. Colvert¹, S. R. Curran², A. Ronald³, D. G. Murphy⁴, R. Goodman¹, F. Happé⁵ and P. F. Bolton¹, (1)*King's College London*, (2)*Kings College London*, (3)*Birkbeck College*, (4)*Institute of Psychiatry, King's College London*, (5)*Institute of Psychiatry, King's College London*

Background: Recent guidelines produced by the National Institute for Health and Clinical Excellence (UK) highlight an increased demand for diagnostic services for children and adults with Autism Spectrum Disorder (ASD) as a result of an increase in reported prevalence to at least 1% of the population (NICE clinical guidance 128 & 142, 2011 & 2012). 'Gold standard' diagnostic tools such as the Autism Diagnostic Interview (ADI-R) and Autism Diagnostic Observation Schedule (ADOS) are cost and time intensive and are therefore difficult to use in community settings. There is a need to develop ASD assessment tools that can be used in these settings. The Development and Well-Being Assessment (DAWBA) is an online package of questionnaires that can be administered online or by interview. It covers a range of psychiatric disorders and generates probabilities that an individual has each disorder. A clinician reviews all information to confirm diagnoses.

Objectives: The aim of this study was to test the validity of the ASD module of the Development and Well-Being Assessment (DAWBA) in identifying cases of ASD in a community sample of adolescent twins. Information from the Social Aptitude Scale (SAS) and Strengths and Difficulties Questionnaire (SDQ), which are both included in the DAWBA package, was also used to help identify cases.

Methods: The sample consisted of 285 adolescents selected from the Twins Early

Development Study (TEDS) and included children who had been identified as being at risk of ASD (score of ≥ 15 on the Childhood Autism Spectrum Test (CAST) or ASD label given by healthcare or education professional), co-twins of children at risk of ASD, and low risk controls (CAST score < 12). Parents completed the ASD module of the DAWBA by telephone interview or online. Families were then visited at home and the ADI-R and ADOS were used by the research team to generate a consensus diagnosis of ASD.

Results: DAWBA ASD symptom scores correlated highly with ADI-R algorithm scores ($\rho = .82$, $p < .001$). Good sensitivity and specificity were achieved using computer generated probability bands (sensitivity = 0.86, specificity = 0.94). Using clinician reviewed DAWBA diagnosis improved specificity but sensitivity was lower (sensitivity = 0.77, specificity = 1.00). Sensitivity could be improved if other information in the DAWBA package (Peer Problems and Prosocial scores from the SDQ; SAS scores) was utilised alongside clinician reviewed diagnosis (sensitivity = 0.82, specificity = 0.97). Positive predictive value ranged from 0.97 to 1.00 and negative predictive value from 0.81 to 0.89.

Conclusions: Results suggest that the DAWBA could be used to identify cases of ASD in samples of relatively straightforward cases of ASD and clear-cut non-cases. High confidence is warranted in positively identified cases, though the DAWBA appears to perform somewhat conservatively and misses some cases. Using SDQ and SAS scores can help to identify some of these missed cases. The DAWBA may therefore be useful in community settings, where many cases are likely to be straightforward and when it is impractical to use the ADI-R.

107.088 88 The Suitability of Self-Report Measures for Adult Autism Spectrum Disorder Diagnoses. C. K. Holmes^{*1} and R. L. Young², (1)*Flinders University*, (2)*Flinders University of South Australia*

Background:

Parent report and behavioural observation tools are commonly used to assist with diagnosing autism spectrum disorders in childhood. However, in adulthood, these tools can be inappropriate and impractical. Self-report tools have been developed to address such limitations but rely upon insight

into one's impairments, which may be influenced by theory of mind, social impairments and intellectual functioning. The suitability of these tools for adults with autism spectrum disorder diagnoses thus remains unclear.

Objectives:

The aim of this study was to evaluate the diagnostic performance of commonly used self-report questionnaires among adults with Asperger disorder and whether theory of mind, intellect and social impairments influenced the insight required to effectively use these tools.

Methods:

51 adults with Asperger's disorder and 25 adults without an autism spectrum disorder participated. Each participant completed the Ritvo Autism Asperger Diagnostic Scale-Revised (RAADS-R) and Autism-Spectrum Quotient (AQ). For each self-report questionnaire, standardised scores were calculated to reflect the extent of symptomatology reported. Scores for persons with Asperger's disorder were then compared to standardised ratings of their symptomatology made by clinicians using the Autism Diagnostic Observation Schedule-Generic and DSM-IV-TR checklist for Asperger's disorder and parents, spouses or caregivers who completed the Social Communication Questionnaire. Theory of mind, intellectual functioning (as indexed by verbal comprehension and perceptual reasoning), and social impairments were assessed using the social criteria from the DSM-IV-TR checklist and shortened forms of the Strange Stories Test and Wechsler Adult Intelligence Scale, fourth edition respectively. Moderated regressions were used to determine whether theory of mind, social impairments and intellect predicted one's ability to accurately report one's symptomatology (self-reporting insight); the degree of discrepancy between self and other rated symptomatology. The diagnostic performance of the self-report questionnaires was also assessed.

Results:

The RAADS-R had adequate sensitivity (.91) and specificity (.84). When using a cut-off of 26, the AQ performed with adequate sensitivity (.85) and

specificity (.96). However, using the original cut-off of 32, sensitivity was reduced (.58) despite perfect specificity.

It was noted that some adults with Asperger's Disorder substantially under or over-reported the extent of their symptomatology relative to clinicians, parents, caregivers and spouses. However, on average these discrepancies were slight. Collectively, social impairments, theory of mind and intellect were significant predictors of self-reporting insight evaluated against the DSM-IV-TR checklist and SCQ. The most consistent unique predictors of self-reporting insight for the AQ were social impairments and theory of mind. For the RAADS-R, the most consistent unique predictor of self-reporting insight was non-verbal IQ as indexed by perceptual reasoning ability.

Conclusions:

This study provides further support for the diagnostic suitability of the RAADS-R (Ritvo et al., 2010) and provides support for recommending a cut-off of 26 with the AQ (c.f. Woodbury-Smith, et al., 2005). Nevertheless, disparity in the ability to self-report among adults with Asperger's disorder, which can be influenced by intellect, social impairments and theory of mind, may limit the suitability of self-report diagnostic measures for some individuals. Therefore, these tools should not be used in isolation when making diagnostic decisions.

107.089 89 Using the Quantitative Checklist for Autism in Toddlers (Q-CHAT) At 24 Months to Predict ASD Diagnosis At 36 Months. G. Pasco*¹, K. Hudry², S. Chandler¹, C. Allison³, S. Baron-Cohen³, M. Elsabbagh⁴, M. H. Johnson⁵ and T. Charman¹,
(1)*Institute of Education*, (2)*La Trobe University*, (3)*University of Cambridge*, (4)*McGill University*, (5)*Birkbeck, University of London*

Background:

The British Autism Study of Infant Siblings (BASIS) is a longitudinal study involving participants with older siblings with a diagnosis of ASD (high-risk sibs) and controls with no older siblings with ASD (low-risk sibs). Participants were assessed at 6, 12, 24 and 36 months, using a range of standardised, observational and questionnaire measures. The Quantitative

Checklist for Autism in Toddlers (Q-CHAT) is a normally-distributed 25-item questionnaire designed to be completed by caregivers of children at approximately 18 to 24 months. Scores for each item range from 0 to 4, with higher scores representing a greater level of traits associated with the autism spectrum. Total scores are calculated by summing scores from all items.

Objectives:

To investigate the predictive validity of administering the Q-CHAT at 24 months in a high-risk sample and to identify Q-CHAT items that may function as red flags for autism.

Methods:

The Q-CHAT was completed by parents of high-risk (N=49) and low-risk (N=47) participants just prior to the 24-month assessment (mean 23.9 months, SD 1.0). Following the 36-month assessment (mean 37.9 months, SD 3.1) children in the high-risk group were assigned to one of three subgroups based on a best estimate clinical diagnosis: *Typically developing* (Sib-TD; N=23); *ASD* (Sib-ASD; N=15); and *Other concerns*(Sib-Other; N=12) – children who appeared to have some developmental difficulties but who did not meet criteria for ASD.

Results:

There was no significant difference between the Q-CHAT total scores of the high- and low-risk groups ($t=-1.48$, $p=0.14$). Total scores of the Sib-ASD group were significantly higher than those of Sib-TD ($p<0.01$) and Sib-Other ($p<.05$) subgroups and the low-risk group ($p<.01$), but there were no differences between the three non-ASD groups. Individual items with scores of "3" or "4" in more than 25% of each subgroup were identified. Seven items were identified from the Sib-ASD group, relating to *echolalia* (73%); *using another's hand as a tool* (67%); *repetitive behaviour* (47%); *offering comfort* (33%); *lining up objects* (27%); *staring at a spinning object* (27%); and *sniffing or licking unusual objects* (27%). The *echolalia* item was endorsed by 39% of parents in the Sib-TD group, and the item relating to *using another's hand as a tool* by 40% of parents in the low-risk group. The mean

number of these red flags in the Sib-ASD subgroup was 3.0 (SD = 2.1), significantly greater than in each of the other groups, which did not differ from each other.

Conclusions:

Q-CHAT total scores at 24 months are potentially predictive of ASD status a year later. Furthermore, some specific items, relating primarily to a range of repetitive and stereotyped behaviours, may be sufficiently sensitive to act as red flags for ASD. Further validation in other whole population samples is ongoing.

107.090 90 An Eye-Tracking Based Diagnostic Screener for Autism Spectrum Disorders in 18- to 42-Month-Old Children. M. Valente*¹, M. Ly², A. Klin¹ and W. Jones¹, (1)Marcus Autism Center, Children's Healthcare of Atlanta & Emory University School of Medicine, (2)Marcus Autism Center,

Background: Mean age of diagnosis for an autism spectrum disorder (ASD) in the United States is currently later than five years of age. This late age marks the loss of a potentially critical opportunity for improving treatment efficacy and associated outcome. In addition, gold standard diagnostic evaluations usually require multiple tests proctored by an experienced clinician at specialized centers. These are not often available in either rural or disadvantaged communities, and primary care providers are hesitant to recommend such tests without being certain of initial concerns. In order to improve the efficacy of early screening, new tools yielding objective, performance-based measures of risk for autism would be highly advantageous. Past research using eye-tracking has shown evidence of strong between-group differences when comparing children with ASD to their typically-developing (TD) peers, with large effect sizes. In some cases, the eye-tracking measures have demonstrated predictive utility for measuring individual levels of social-communicative disability. In the current research, we tested the utility of eye-tracking as a screener for ASD in 18- to 42-month-old children.

Objectives: The objective of this research is to test the extent to which patterns of dynamic visual scanning in 18- to 42-month-old children, measured by eye-tracking, can serve as a screening tool, with sensitivity and specificity

values above the accepted range for first-level screeners (>80% per Meisels, 1989). We also tested the procedure's ability to quantify levels of social and communicative disability in individual children.

Methods: Eye-tracking data were collected from a large cohort of children, N = 170, 18 to 42 months of age, while they watched naturalistic video scenes of peer social interaction. Standardized clinical assessment measures (ADOS, ADI, cognitive and language testing) confirmed diagnostic status for ASD and TD children within the cohort. The first 50 consecutive referrals in the ASD group (ASD-1) were used for comparison against the TD group; these children provided a training set with which to develop a model of expected differences between ASD and TD visual scanning. We then tested the remaining ASD children (ASD-2) as an external validation sample. Receiver operating characteristic (ROC) curves were created to analyze sensitivity and specificity.

Results: Preliminary results indicate robust between-group differences in visual scanning between TD and ASD-1 groups. Using this model, the remaining ASD-2 children were classified with sensitivity of 85% and specificity of 77.9%.

Conclusions: This research demonstrates a first step towards an eye-tracking based diagnostic screener intended for children between 18 and 42 months. Further research will test the extent to which such a screener can be optimized and practically deployed.

107.091 91 Late Diagnosis of Autism Spectrum Disorder – Missed or Over-Diagnosed?. M. Davidovitch* and D. Golan, *Maccabi Healthcare Services*

Background: Currently, nearly 30% of children in Maccabi Healthcare Services are diagnosed with Autism Spectrum Disorder (ASD) after the age of six years. Although the high rate of late diagnosis could be due to sparse symptoms or lack of ASD awareness, many children with late diagnoses underwent initial evaluations at a Child Developmental Center (CDC) when they were younger.

Objectives: To characterize children who were evaluated at a young age in the Child

Developmental Center, did not receive an ASD diagnosis, and were later diagnosed with ASD by a child neurologist or psychiatrist.

Methods: A search of the Maccabi Healthcare Services computer registry was conducted for children who were diagnosed with ASD between 2004 and 2010 after the age of 6 years. All records were checked by the authors to eliminate technical errors and to confirm the age of ASD diagnosis. Data was collected for children who prior to age six were evaluated at Maccabi's CDC in four areas: developmental pediatrics, psychology, speech language pathology and occupational therapy. Relevant information included the age of child during evaluations as well as developmental diagnoses made by the CDC team. Evaluation summaries were searched for evidence of communication problems (such as abnormal eye contact or abnormal social development) and the children were subsequently divided into four groups: Group 1 – no record of CDC evaluation; Group 2 – no evidence of communication problems in CDC evaluations; Group 3 – some CDC evaluations contained evidence of communication problems, while others did not; and Group 4 – all CDC evaluations contained evidence of communication problems.

Results: Children who met the research criteria (n=159) had a mean age of ASD diagnosis of 93.4 months (16.1 SD). Group 1 contained 51 children. Of the remaining 108 children, Group 2 included 71 children that had 290 evaluations at a mean age of 44.8 months. The three leading diagnoses were language deficits, global delay, and attention problems. Group 3 included 32 children that had 188 evaluations at a mean age of 43.9 months. In 126 evaluations no clues for communication problems was found. Group 4 included 5 children that had 17 evaluations at a mean age of 46.3 months. The leading diagnoses for groups 3 and 4 were language deficits, behavior problems, and global delay. Altogether, out of 495 total evaluations from children in groups 2, 3, and 4, only 79 evaluations (16%) contained a mention of a communication problem.

Conclusions: Two-thirds of the children diagnosed after six years of age were evaluated at an early stage by a multidisciplinary developmental team at the CDC but did not receive an ASD diagnosis. In the majority of evaluations, clues of

communication problems could not be found. The discrepancy between early and late diagnosis figures call into question the reliability of later diagnoses, which in contrast to CDC evaluations, are not made following comprehensive evaluations from a developmental team.

107.092 92 Comparison of ADOS to ADOS-2 Diagnostic Classifications within the Autism Treatment Network. A. Fedele*¹, A. Abbacchi¹ and S. M. Kanne², (1)*Autism Speaks*, (2)*Thompson Center for Autism and Neurodevelopmental Disorders, University of Missouri*

Background: The ADOS (a "gold standard" diagnostic tool for evaluating autism) is a semi-structured, standardized assessment comprised of 4 modules each targeting an individual's expressive language and chronological age. The ADOS assesses communication, social, and repetitive behaviors. The recently published ADOS-2 allows for improved psychometrics and diagnostic algorithms and has expanded to include a Toddler module. It can be administered to anyone suspected of having autism with a non-verbal mental age of at least 12 months to adulthood. Clinicians in the Autism Treatment Network (ATN) were interested in evaluating whether the new algorithms change the classification results on the ADOS. On the previous version, an autism spectrum diagnosis required that the subject meet three cutoffs: social, communication, and social and communication combined. The newly revised algorithm on the ADOS-2 requires that the subject only meet one cutoff: a combination of social affect and restricted and repetitive behaviors.

Objectives: The purpose of the current study was to compare the categorical designations across the ADOS and the ADOS-2 in a very large sample of individuals diagnosed with ASD.

Methods: The ADOS was administered to 5062 children between the ages of 2 and 17 years while participating in the ATN (2237 module 1s, 1197 module 2s, and 1528 module 3s). Coding from the original ADOS data were used to compute the total scores on the ADOS-2 and determine the individual's new cut-offs. As Module 4 does not have a new algorithm, this module was not examined in the current study.

Results: Across modules, the percentage of children who met autism diagnostic cutoffs

increased from 68.7% on the ADOS to 87.4% on the ADOS-2. The percentage of children who met cutoffs for autism spectrum decreased from 24.6% on the ADOS to 8.9% on the ADOS-2. The percentage of those that had not reached cutoffs on the ADOS but were still diagnosed with an ASD by the ATN clinician decreased from 6.7% to 3.8%. The diagnoses of 99% of children with autism did not change when using the ADOS-2 cutoffs, 25% with autism spectrum did not change, and 41% of those with no diagnosis did not change. Similarly, 71% of those with an autism spectrum diagnosis changed to autism, and 60% of those with no diagnosis changed to either autism spectrum or autism. In contrast, 1% of those with autism or autism spectrum lost their diagnosis, and .6% of those with autism moved to autism spectrum. Chi-squares were conducted on all modules combined and for each module separately. The chi-square for all modules combined was highly significant, $X^2 = 2568.8$, $df=4$, $p<.0001$. Likewise, results were significant for each module independently: Module 1 $X^2 = 1136.9$, $df=4$, $p<.0001$; Module 2 $X^2 = 542.8$, $df=4$, $p<.0001$; Module 3 $X^2 = 840.5$, $df=4$, $p<.0001$.

Conclusions: These results indicate that the new ADOS-2 algorithms preserve caseness with respect to an ASD diagnosis. However, the results also indicate a clear shift to a classification that is more definitive (i.e., a shift to a higher level of severity) with regard to the presence of autism.

107.093 93 Early Social Cognitive Development and Behavioural Signs of Autism in Very Preterm Infants. C. L. Sanderson*¹, L. Platten-Brown², D. H. Skuse³ and N. Marlow², (1)*UCL Institute of Child Health*, (2)*UCL Institute for Women's Health*, (3)*Institute of Child Health, UCL*

Background: Children born preterm or at low birth weight are at an elevated risk for autism spectrum disorder (ASD) (Johnson et al., 2010). Toddler parent report measures (e.g. M-CHAT) have revealed very high positive screening rates amongst very preterm (VP) infants (approximately 25%), and direct measures of early symptomology (e.g. Autism Observation Scale for Infants or AOSI) have indicated scores in a similar range to infant siblings later diagnosed with autism. However, given the frequency of cognitive, motor, language and sensory impairment in VP populations, it is difficult to infer

whether these elevated scores truly reflect an early autism phenotype. This study seeks to investigate whether early behavioural signs of autism in VP infants (using the AOSI) are associated with other social cognitive features of the broader autism phenotype (e.g. differential neural responses to direct gaze) and/or developmental delay.

Objectives: To evaluate group differences between very preterm and full term infants in early symptomatology related to ASD (AOSI) at 6 and 12 months gestationally corrected age (GCA) and infants' neural responses (event-related potentials [ERP]) to direct versus averted gaze at 6m. Also, to examine associations between AOSI score, gaze ERP and infants' general cognitive, motor and language development (Bayley III) at 12m.

Methods: Early behavioural signs of ASD were measured in VP infants (25-31 weeks GCA) and full term controls (37-42 weeks) with no family history of ASD at both 6 and 12 months using the AOSI assessment. Total scores and total 'marker' counts (i.e., items scored non-zero) were computed for each child. At 6m, infants' ERPs were recorded in response to viewing faces with eye gaze directed toward versus away from the infant. Analyses included various relevant components in the ERP (P1, N290 and P400). Developmental functioning (cognitive, motor and expressive/receptive language) was measured at 12 months for both preterm and full-term infants using the Bayley III assessment.

Results: Preliminary results from 15 full term and 9 VP infants indicate that relative to full term controls, VP infants show more early behavioural signs (higher Total Scores and more Markers) of ASD on the AOSI. Higher AOSI scores amongst VP infants are associated with lower developmental functioning scores on the Bayley III, but not with abnormal evoked responses to dynamic gaze shifts.

Conclusions: Within the first year, preterm infants show more behavioural signs associated with ASD on the AOSI, demonstrating scores in a similar range to high-risk siblings later diagnosed with ASD. However, higher AOSI scores in VP infants may reflect more non-specific behaviours associated with developmental delay, rather than

a true early autism phenotype. Further follow-up will be important to distinguish whether behavioural abnormalities predict later ASD symptoms/diagnoses *and/or* non-ASD related impairments in this VP cohort.

107.094 94 Child and Family Characteristics That Affect the Clinical Utility of the Modified Checklist for Autism in Toddlers As a Level II Screening Tool in Singapore. H. C. Koh^{*1}, S. Lim², G. Chan², H. H. Lim¹, S. Choo¹ and I. Magiati², (1)KK Women's and Children's Hospital, (2)National University of Singapore

Background: The Modified Checklist for Autism in Toddlers (M-CHAT) is a 23 item parent questionnaire that was developed in the United States, to screen for Autism Spectrum Disorders (ASD) in 16-30 month olds. The M-CHAT is being used as a level II screening tool for developmentally at-risk children up to 48 months old, at a child development specialist clinic in Singapore. The M-CHAT has shown good clinical utility for the Singaporean high risk sample (Koh et al., in preparation). With the 18-30 month olds, the critical (failing 2/6 selected items) and Best7 (failing 2/7 selected items) scoring methods, detected a good majority of children with ASD, without inflating the false positive rate. With the >30-48 month olds, the non-critical (failing 3/23 items) scoring method was more accurate and less likely to miss those with ASD.

Objectives: This study examined the clinical utility of the M-CHAT by investigating child and family characteristics that may affect accuracy of the M-CHAT screening results.

Methods: Parents/caregivers of new patients were asked to complete an intake questionnaire, which included the M-CHAT, before their child's first evaluation by a paediatrician. Medical records of 18-48 month olds seen between February 2009 and July 2010, whose parents/caregivers completed the M-CHAT ($N=580$), were reviewed. Children suspected to have ASD were referred for an ASD diagnostic assessment. For the children who received a diagnosis of ASD ($N=198$), Mann-Whitney and Chi-squared analyses were conducted to determine if there were significant differences between those identified accurately by the M-CHAT and those who were not, on i) measures of ASD severity and overall adaptive functioning of the child; and ii) family characteristics (such as educational level of

parents). For the children who were not diagnosed with ASD ($N=382$), logistic regression analyses were conducted to determine if family characteristics predicted the accuracy of the M-CHAT results.

Results: The children with ASD who were identified accurately on the M-CHAT, had significantly higher ASD severity (non-critical: $U=535.5$, $p<0.001$; critical: $U=780.0$, $p<0.001$; Best7: $U=825.5$, $p<0.001$) and lower overall adaptive functioning (non-critical: $U=372.0$, $p<0.001$; critical: $U=963.5$, $p<0.001$; Best7: $U=858.0$, $p<0.001$), than those who were not. There were no significant group differences in family characteristics for the children with ASD. For the children without ASD, lower educational level of the parents was associated with more false positives on the M-CHAT than true negatives when using the non-critical scoring method ($p=0.001$).

Conclusions: The children with more severe ASD symptomatology and lower overall adaptive functioning are more likely to be detected on the M-CHAT. The accuracy of the M-CHAT for detecting children with ASD appears to be unaffected by demographic characteristics of the children's parents. For the children without ASD, there were higher false positive rates when parents of lower educational levels completed the M-CHAT. These parents may have poorer understanding of the questions on the M-CHAT or of the importance of observing early social and communication behaviours in their young children. Parents may need to be better educated on child development, so that they can be better aware of typical versus atypical early development in their children.

107.095 95 The Validation of the 3DI-Sva As a Diagnostic Tool for Autistic Spectrum Disorder. J. Wakefield^{*1}, D. H. Skuse², K. Lawrence³ and W. Mandy⁴, (1)UCL Institute of Child Health, (2)Institute of Child Health, UCL, (3)Royal Holloway, (4)Faculty of Brain Sciences, UCL

Background: The diagnosis of autistic spectrum disorder (ASD) requires the integration of information from multiple sources regarding social communication, language and repetitive stereotyped behaviours. Many adults with an ASD are not appropriately diagnosed in childhood. Efficient and accurate tools that can be utilised

with adults to detect current clinical features in addition to those present in development are required to facilitate accurate diagnoses in adults.

The Dimensional, Developmental and Diagnostic Interview (3DI) is a parental interview designed to assess children's behaviour and provide an accurate tool for scoring and interpretation. It has high test-retest and inter-rater reliability and accurately distinguishes between children with ASD and those with non-ASD disorders.

The Dimensional, Developmental and Diagnostic Interview: short form for adults (3DI-sva) has been developed to provide quick and accurate diagnostic information regarding adults. It consists of 73 items covering three subscales (Social, Communication and Repetitive Stereotyped Behaviours), including four items on early development and is administered to the parents of adults being assessed for an ASD.

Objectives: This study has two aims.

1. To validate the 3DI-sva as a tool for accurately discriminating between typically developing adults and those with an ASD.
2. To quantify appropriate minimum cut points for each subscale that would define an adult as being likely to have an ASD.

Methods: In total, forty-six adults and one of their parents/carers were recruited. This consisted of thirty-three typically developing adults (17 males and 16 females) and thirteen adults with an established diagnosis of ASD.

Four interviewers were trained in the appropriate administration and coding of the 3DI-sva and they interviewed parents/carers of typically developing subjects by telephone. Each rater transcribed four of their interviews for subsequent inter-rater reliability analysis. Parents/carers for the ASD group were interviewed by telephone by one researcher only.

Results: The mean ages in years (and standard deviations) of the groups were as follows; ASD 23.12 (3.92), typically developing males 23.24 (3.73) and typically developing females 21.81 (2.64).

Telephone interviews took forty-five minutes to complete.

Interviews for typically developing samples had inter-rater reliability scores over 0.98 as calculated by Pearson's Correlation Coefficient.

Cronbach's alpha was calculated to measure internal consistency of the three subscales and was above 0.7 for all domains across both groups with the exception of the communication domain in the ASD group (0.683). All the original interview items were therefore retained.

ASD subjects scored significantly higher than typically developing adults across all three domains as calculated using a one-way multivariate analysis of variance (MANOVA).

Receiver operating characteristic curves were utilised to calculate cut off points to discriminate between typically developing and ASD adults. The 3DI-sva demonstrated an ability to discriminate with a sensitivity of 1 and a specificity of 0.87.

Conclusions: The 3DI-sva is quick to use, has good inter-rater reliability, provides dimensional ratings of symptom severity and effectively discriminates between typically developing and ASD adults across all three subscales associated with a diagnosis of ASD.

It therefore has important utility as a diagnostic tool for adults.

107.096 96 MCHAT-R Screener Predictive Validity in a High-Risk Infant Sibling Population. H. Noble*¹, A. S. Weitlauf², W. A. Loring³, A. Nicholson³, J. A. Crittendon², C. R. Newsom³ and Z. Warren², (1)TRIAD, Vanderbilt Kennedy Center, (2)Vanderbilt Kennedy Center, (3)Vanderbilt University

MCHAT-R Screener Predictive Validity in a High-Risk Infant Sibling Population

Background: Recent work suggests that the risk of recurrence of ASD in younger siblings of diagnosed children may be as high as 18.7% (Ozonoff et al., 2011). Given the elevated prevalence rates in siblings and potential genetic contributions to ASD symptomatology (Szatmari et al., 2007), effectively screening infant siblings is of high importance to clinicians and families.

However, the neurodevelopmental complexity of this population (e.g., elevated rates of non-ASD concerns, broader phenotype concerns, patterns of resiliency despite early delays) effectively screening siblings regarding ASD specific risk is a challenging process

Objectives: The purpose of this study was to determine if a screening tool alone is sufficient to detect an "at risk" diagnosis for ASDs in Sibs-ASD. We did this by evaluating children who passed the MCHAT-R within the context of a comprehensive psychological evaluation.

Methods: Participants included 37 infant siblings of children diagnosed with an autism spectrum disorder (Sibs-ASD). Potential participants in a larger study who passed a screening with the MCHAT-R between 16 and 30 months of age were invited to participate in a cost-free developmental evaluation between ages 16-42 months. This evaluation included a thorough developmental history, a DSM-IV structured clinical interview, and cognitive (Mullen Scales of Early Learning), social-communication (Autism Diagnostic Observation Schedule), and adaptive behavior (Vineland Adaptive Behavior Scales – II, Communication and Social domains) testing.

Results: Approximately 38% of the sample (14/38) received a neurodevelopmental diagnosis at follow-up. Specifically, 19% (n=7) of Sibs-ASD who passed the MCHAT-R received an ASD diagnosis. An additional 19% (n=7) received other diagnoses, including developmental or language delay (n=5) and "at risk" for ASD (n=2). Post-hoc Tukey tests of one way ANOVAs revealed that participants who received an ASD diagnosis had significantly higher Calibrated Severity Scores (Gotham et al., 2010) than participants with no diagnosis ($p < .05$). No Diagnosis participants had significantly higher scores on Mullen Receptive and Expressive language than other participant groups ($p < .05$). No Diagnosis participants scored higher ($p < .05$) on measures of nonverbal problem solving than Other Diagnosis but not ASD participants. No differences emerged between groups on Vineland Communication or Social domains.

Conclusions: Siblings of children with ASD are a complex population and therefore may require a more stringent diagnostic process for determining

if they are actually "at risk" for an autism spectrum disorder. While some siblings with ASD will likely be captured a relatively small, but clinically meaningful percentage will not be detected via use of this instrument alone. Given the high recurrence rate of ASD and other developmental concerns, clinicians and practice organizations may need to advocate for more in depth evaluation of siblings of children with ASD as standard practice rather than a follow-up to simple screening.

107.098 98 Language Impairment in Younger Siblings of Children with ASD: Stability and Predictors. K. Sheperd^{*1}, P. Rao² and R. Landa³, (1)*The Johns Hopkins University School of Medicine*, (2)*Kennedy Krieger*, (3)*Kennedy Krieger Institute*

Background:

Language impairment is common in ASD, yet some show typical language functioning at school-age. In addition, early language delay has been reported in Non-ASD siblings of children with ASD (sibs-Non-ASD).

Objectives:

To define:

1. stability of early language delay in sibs-ASD and sibs-Non-ASD.
2. very early predictors of later language impairment in younger siblings of children with ASD.

Methods:

Participants were 132 younger siblings of children with ASD enrolled in a prospective, longitudinal study. Outcome classification of ASD (n=25) versus Non-ASD (n=107) was determined at age 36 months. Language assessments were conducted at ages 14, 24, and 36 months using the Mullen Scales of Early Learning (MSEL; Mullen, 1995) Receptive (RL) and Expressive Language (EL) scales, and at 4 to 8 years using the Test of Oral Language Development-P3 (TOLD-P3; Newcomer & Hammill, 1997). Early language delay was defined as scoring > 1.5 standard deviations below the test mean on the MSEL RL or EL scale. The 'gold standard'

language delay classification was defined by scores of >1.5 standard deviations below the test mean on any TOLD-P3 subtest at school-age. Children with ASD were only included in analyses if they completed the TOLD-P3.

To define early predictors of school-age language impairment, we examined frequency of initiation of joint attention (IJA) and inventory of gestures using the Communication and Symbolic Behavior Scales Developmental Profile (CSBS; Wetherby & Prizant, 2002), MSEL Visual Reception (VR) and RL and EL T scores, and ADOS-G Communication algorithm score (Lord et al., 1999) at age 14 months.

Results:

At 14 months, 68% of the ASD group and 38% of the Non-ASD group had language delay. By school-age, 58% and 14% of the ASD and Non-ASD groups, respectively, had language delay.

In the ASD group, 66% of 14-month-olds with language delay also met TOLD-P3 criteria for language delay at school-age. Sensitivity (.71) of language delay on the MSEL improved marginally by age 36 months. In contrast, specificity of language delay on the MSEL at age 14 months was very poor (.30). By age 24 months, specificity reached .70, and was maintained at that level through age 36 months in the ASD group.

For the Non-ASD group at 14 months, sensitivity and specificity of language delay classification per the MSEL were .53 and .64, respectively. Sensitivity continued to drop through age 36 months (.21 and .14 at 24 and 36 months, respectively), while specificity reached a high level (.91) by 24 months, and was sustained through 36 months (.98).

At age 14 months, VR and IJA scores were the best predictors of language impairment at school-age ($X^2 = 9.96$; $p = .002$), explaining 25% of the variance. The individual outcome classification rate was moderate to high (83.5%), with good sensitivity (.75) and specificity (.84).

Conclusions:

Early language delay is transient in many Non-ASD-sibs-A. Some ASD-sibs-A acquired early language milestones but exhibited delays in later syntactic and semantic development. Nonverbal cognition and joint attention are better early predictors of school-age language delay than early language skills in sibs-A.

107.099 99 Developmental Surveillance Versus Screening for the Identification of Autism Spectrum Disorders in Infants and Toddlers. J. Barbaro*, A. Mitchell and C. Dissanayake, *La Trobe University*

Background: Despite the importance of early detection and intervention for children with Autism Spectrum Disorders (ASDs), there are currently no screening tools with sufficient psychometric properties that can be recommended for universal use. Barbaro and Dissanayake (2010) utilised a developmental surveillance framework in the Social Attention and Communication Study (SACS) to prospectively identify infants and toddlers with ASDs. The SACS was accurate and sensitive in the identification of ASDs from 12- to 24-months of age. They argued that this was a result of: 1) utilising repeated monitoring within a developmental surveillance framework, rather than 'once-off' screening at a particular age; and 2) the use of skilled observations, rather than sole reliance on parental report. The current study aimed to test these arguments.

Objectives: The first aim in the current study was to compare the psychometric properties of the SACS to several screening tools in identifying infants and toddlers 'at risk' for ASDs, in the same sample of children. The second aim was to examine the consistency of parental reporting of children's behaviours across different ASD screening questionnaires. The third aim was to examine agreement between parental reporting on these questionnaires and skilled professional observations of the same behaviours.

Methods: Participants were drawn from the SACS sample ($n = 110$), and comprised children who were assessed at least once at 12-months ($n = 10$), or 18-months ($n = 46$). The screening tools utilised at these assessments included the First Year Inventory (FYI), the Communication and Symbolic Behavior Scales-Developmental Profile (CSBS-DP), the Checklist for Autism in Toddlers (CHAT), the Modified- CHAT (M-CHAT), and the

Early Development Interview (EDI). The psychometric properties of these tools were calculated and compared to those of the SACS, reported in Barbaro and Dissanayake (2010). Furthermore, responses on items measuring the same behaviours across the different parental report tools were compared. Additionally, these same responses were also compared to skilled observations of the same behaviours in the SACS.

Results: Results indicated that the SACS demonstrated a better balance between good to excellent specificity, sensitivity, and positive predictive value compared to each of the screening tools, which consistently traded specificity for sensitivity, or vice versa. Furthermore, consistency of parental report on items measuring the same behavioural construct, across different screening tools, was poor, with only 9 out of 26 associations (35%) at 12-months, and 4 out of 12 associations at 18-months (33%) having acceptable Spearman rho values of .70 or more. Similarly, there were no acceptable correlations of .70 or more between parental report and skilled observations of children's behaviours on the SACS.

Conclusions: The current results confirmed that a development surveillance framework, utilising repeated monitoring of children's behaviours via skilled observations, is more robust than the use of screening tools. This study revealed the variability in parental report of children's behaviours both across different questionnaires and in comparison to skilled observation of the same behaviours. These results highlight possible reasons for the lack of screening tools for ASDs with sufficient psychometric properties to be recommended universally.

107.100 100 Comparative Profiles of Late Preterm and Full Term Male Toddlers with Autism. K. E. Caravella*¹, T. Cermak² and C. Klaiman¹, (1)*Marcus Autism Center, Children's Healthcare of Atlanta & Emory University School of Medicine*, (2)*Marcus Autism Center*

Background:

Previous research has examined autism spectrum disorders (ASD) in extremely preterm infants (23-30 weeks gestational age) and has indicated increased screen positive rates (Limperopoulos et al., 2008) and elevated SCQ and SRS scores (Movsas & Paneth, 2012) indicating higher

likelihood of meeting criteria for an ASD. Additional prospective research has found that extremely preterm infants have higher SCQ scores than term birth peers, regardless of diagnostic status (Johnson et al., 2010). Less is known however about late preterm infants (34-36 weeks gestational age) and its implications for ASD.

Objectives:

This study examined profiles of preterm and term toddlers with a diagnosis of autism. We aimed to further previous research by examining a cohort of children considered at greater risk for developmental delays due to shortened gestational age, however not typically followed as closely as their extremely preterm counterparts. Of greatest interest was the difference in diagnostic profiles of these cohorts before the age of 3.

Methods:

This study included 34 male toddlers, 10 late preterm (mean age 25.36 months) and 24 term (38-41 weeks gestational age, mean age 23.71 months), all diagnosed with Autistic Disorder. All participants were referred based on parent concerns for a first time comprehensive diagnostic evaluation that included the *Mullen Scales of Early Learning*, the *ADOS, Module 1*, and the *Vineland Adaptive Behavior Scales II*.

Results:

ANOVAS were used to compare differences between groups. On the developmental assessments, significant differences were found on the domain of Visual Reception (VR) [$F(1, 32) = 4.717, p < .05$], with preterm toddlers achieving higher scores than term toddlers. With regards to adaptive behavior, significant differences were found on the Daily Living Skills [$F(1, 32) = 11.845, p < .01$], Communication [$F(1, 32) = 7.993, p < .01$], and Socialization [$F(1, 32) = 4.462, p < .05$] domains. All standard scores were higher for late preterm infants. With regard to diagnostic differences, on the ADOS, significant differences were found on social affect domain totals [$F(1, 32) = 5.847, p < .05$], with preterm

toddlers receiving lower social affect totals. No significant differences were found with respect to repetitive behaviors ($p = .90$). When VR is covaried, significant differences still remain.

Conclusions:

This study found that in contrast to previous research supporting elevated symptomatology in extremely preterm children, late preterm toddlers have lower levels of symptomatology as measured by the ADOS social affect total. A point of interest is that restrictive and repetitive behavior (RRB) totals are not significantly different between the two groups, suggesting that for preterm toddlers, their ADOS total scores are more substantially impacted by RRBs, than term toddlers. Additionally, late preterm toddlers have higher visual reception scores, though still below average. Late preterm toddlers are also showing greater adaptive functioning in all domains, with the exception of gross motor. Important future directions include obtaining a larger sample size, and following these toddlers into adolescence to investigate the impact of these early predictors on outcome and level of functioning.

107.101 101 The Diagnostic Odyssey: Parents' Experiences of the Diagnosis of Autism. J. S. Singh*, *Georgia Institute of Technology*

Background: For parents of children diagnosed with autism spectrum disorder (ASD), the diagnosis process can be a time of incredible uncertainty, stress and concern. Despite the growing number of parents receiving a diagnosis of ASD for their child, there is limited understanding about parents' experiences of life before, during, and after receiving an ASD diagnosis.

Objectives: The objectives of this research were to identify the diagnosis process through the perspective of parents who have a child diagnosed with ASD. Based on parents' experiences surrounding their pre-diagnosis concerns, the process of getting a diagnosis, and the post-diagnosis trajectory, this paper details what clinical professionals describe as the diagnostic odyssey. This concept encompasses the processes parents go through to understand the problems their child is experiencing in order to get them the appropriate help they need.

Methods: This paper is based on in-depth semi-structured interviews with parents who have a child diagnosed with autism (N=28). Each interview lasted from 1-2 hours, was tape recorded, transcribed, and coded for major themes using grounded theory methods.

Results: The findings reveal the complexity of the diagnostic odyssey and the struggles and various levels of uncertainty parents experience throughout the diagnosis process. In the pre-diagnosis phase, most parents suspected something was wrong, however their pediatrician, as well as other family members, often did not share their levels of concern. Once a child was given a diagnosis of ASD, parent's described their uncertainties associated with arbitrary labels given to their children such as "*not quite autism*", "*pervasive developmental disorder autistic like*", or "*mild autism*." For most parents, the overwhelming news of an ASD diagnosis was coupled with limited direction on how to proceed in helping their child. Hence, the parents themselves largely drove the post-diagnosis trajectory. Parents emphasized how they had to do their own research, felt there were limited resources they could draw upon, and were responsible for locating, assessing, and coordinating everyone involved in their child's care.

Conclusions: The parents' experiences in the diagnostic odyssey demonstrate a need for an increased focus on educating professionals (e.g., pediatricians, educators, and others) to recognize early signs of autism and be able to refer parents to appropriate diagnostic services. Once the diagnosis is made, there is also a critical need for clear guidelines on how parents should proceed forward despite arbitrary labels and uncertainties in different treatment outcomes. Although there are resources available through national organizations, parents also need help navigating their particular local resources, especially with regard to educational services. Given the rise in ASD prevalence in the last decade, these issues warrant attention from the autism research community.

107.102 102 An Online Delphi Process to Identify ASD Diagnosis Guidelines for Best Practice Evaluation and Implementation. C. Koning*¹, L. Zwaigenbaum², S.

Reynolds¹, V. Guiltner¹ and E. Kelly¹, (1)Glenrose Rehabilitation Hospital, (2)University of Alberta

Background:

Active mobilization of research evidence into clinical practice requires knowledge transfer processes which systematically implement activities which support better outcomes based on clear scientific evidence. Numerous guidelines, based on considerable evidence and expertise, have been developed to describe best practice in the diagnosis of ASD. A large tertiary children's hospital, with approximately 500 ASD query referrals annually, chose an implementation science framework to enable implementation of best practice guidelines. This abstract describes consensus development processes used to identify initial best practice implementation targets.

Objectives:

Report a case study using implementation science principles to adapt and operationalize multiple best practice guidelines to establish an ASD diagnostic model for a tertiary clinic setting.

Methods:

Four rounds of voting facilitated consensus development and decision-making over a 3-month period using a modified Delphi process which combined online and in-person group discussion. The process was designed to be iterative, using data and discussion to modify methodology. Decisions regarding changes were made prior to beginning each round with input from all stakeholders. The Delphi system for choosing best practice guidelines had the following characteristics:

- Representative stakeholders including different disciplines, levels of leadership, researchers and community representatives (n=9).
- Provision of evidence-based background information including ASD guidelines from 1) National Institute for Health and Clinical Excellence, 2) Miriam Foundation's Canadian Best Practice Guidelines, and 3) British Columbia's Standards and

Guidelines for the assessment and diagnosis of ASD.

- Delphi rules/principles included anonymous on-line voting, criteria to guide Likert scale voting and between-round decision-making, between-round data synthesis and presentation, and adaptation of the process based on data synthesis and stakeholder discussion.

Results:

All guidelines were reviewed to determine which had complete consensus. These included a) which professionals could be included in the diagnostic team, b) team competencies, c) need for collaborative communication amongst team members and families, d) need for written documentation, e) need for formal observation and parental interview without reliance on a single diagnostic tool, and f) consideration for co-morbid conditions. Forty-seven guidelines were then used in the next round of online voting. Participants voted using 6 criteria and a 5-point Likert scale. Data from this round resulted in changes to criteria for the next round, changes to the Likert scale, and 20 guidelines for consideration in the next round. A final voting round voting required participants to rank remaining guidelines with the goal of systematically implementing these practices for the diagnosis of all children with a query of ASD. An evaluation plan and implementation process, using the National Implementation Research Network framework, was developed to address implementation of guidelines identified as priorities for ASD diagnosis.

Conclusions:

This strategy was effective in achieving consensus across multiple stakeholders. We propose that implementation science provides an inclusive approach to determining service delivery guidelines and enacting change in a large institution. The implementation science framework will be used to establish evaluation tools for outcomes and implementation process.

107.103 103 Changes On the Horizon: Comparing DSM-5 Autistic Spectrum Disorder with Social Communication Disorder. R. Varrall*¹, D. H. Skuse², J. Wakefield³ and

W. Mandy⁴, (1)*Great Ormond Street Hospital*, (2)*Institute of Child Health, UCL*, (3)*Institute of Child Health at UCL*, (4)*Faculty of Brain Sciences, UCL*

Background: The arrival of DSM-5 heralds a transition in our understanding of neurodevelopmental disorders; a transition which will have consequences beyond the academic and clinical spheres, reaching into the daily lives of individuals receiving a diagnosis. DSM-5 proposes a two domain-based definition of Autism Spectrum Disorder (ASD). These domains comprise: i) social communication deficits; ii) restricted, repetitive patterns of behaviour, interests, and activities plus sensory sensitivities. Criteria require symptoms to limit and impair everyday functioning. Changes from DSM-IV-TR mean those who do not meet criteria in both domains cannot be diagnosed as 'ASD'. A controversial new construct - Social Communication Disorder (SCD) - will apply to many who would have met PDD-NOS criteria under DSM-IV-TR.

Objectives: The study tests the hypothesis that proposed diagnoses of ASD and SCD can be differentiated on measures of adaptive functioning, pragmatic communication and social communication.

Methods: Criteria for both a diagnosis of ASD and of SCD were operationalized on the basis of data from parent-report (3Di), and ADOS. The 3Di was used to emulate the content of both ASD domains and SCD domains, on the basis of 170 phenotypic items drawn from our computerized database. SCD was defined first by exclusion (not ASD) and second, on basis of scores in the clinical-range on the composite pragmatic language scale of the Children's Communication Checklist (CCC). Final ASD group; N=43, mean age = 10.6 yrs; SCD group; N=15, mean age = 11.50 yrs. Measures of cognitive ability included WPPSI or WISC. Vineland Adaptive Behaviour Scales (parent-rated) measured adaptive functioning.

Results: Participants were matched for age and IQ. Results demonstrated no significant differences in adaptive functioning existed between the ASD and SCD groups. Both diagnostic groups demonstrated clinically significant levels of impairment relative to population norms. On CCC-based measures of

communicative competence (5 subscales, measuring inappropriate initiation, coherence, stereotyped conversation, use of context, and rapport), there were no significant differences between group scores on any subscale. Social communication skills were measured by both parent report (3Di) and by direct observation (ADOS). Parent report found no significant differences between groups, but those with ASD had significantly greater communication impairment as measured by the ADOS.

Conclusions: Young people meeting diagnostic criteria for ASD and SCD have significant impairments in adaptive functioning as well as poor pragmatic communication skills. Direct observation revealed greater impairments in the communication domain of the ADOS in those with ASD (i.e. who met both A and B-scale criteria under DSM-5). Adaptive functioning was similarly impaired in all domains, in both diagnostic groups.

107.104 104 Diagnostic Validity of the ADOS and ADI-R in Children Aged <48 Months: A European Perspective. E. Zander*¹, H. Sturm¹ and S. Bölte², (1)*Child and Adolescent Psychiatry, Stockholm County Council*, (2)*Karolinska Institutet*

Background: The diagnostic validity of the ADOS (revised algorithms) and the ADI-R (research algorithms) for ASD in young children with developmental difficulties has been studied in research settings in the USA (e.g. Kim & Lord, 2012). However, less is known about the validity of the gold standard in early childhood populations in clinical settings and in other countries.

Objectives: To examine the diagnostic validity of the ADOS (revised algorithms) and ADI-R (research algorithms) in a clinical child psychiatric out-patient unit in Stockholm, Sweden.

Methods: All children with unclear developmental problems (aged <48 months) assessed between 2007 and 2012 at the Neuropsychiatric Unit South East, Stockholm County (www.childdevelopment.se) were included in the study ($N > 200$; ~25% girls; ~60% of Swedish origin, 30% of non-European origin). Aside from the ADOS and ADI-R the assessments included the Vineland-II, Merrill-Palmer-R/Mullen Early Learning Scales and observations in the children's

preschool. Diagnostic validity of the ADOS and ADI-R was investigated against a best estimate clinical consensus diagnosis made by an experienced clinical team (child psychiatrist, psychologist, social worker).

Results: About 70% of the referred children were diagnosed with ASD; the remainder primarily with ADHD and intellectual disability. The ADOS (sensitivity: 96%; specificity: 64%) had a higher diagnostic accuracy than the ADI-R (sensitivity: 58%; specificity: 78%).

Conclusions: Both ADOS and ADI-R provide clinically valuable information in the assessment of young children with a suspected ASD. Overall, the ADOS showed a higher diagnostic validity than the ADI-R, although the interview yielded a somewhat higher specificity than the ADOS in a European clinical outpatient unit.

107.105 105 Rating Scale Measures Are Correlated with Automated Video Tracking of Behaviors of Children On the Autism Spectrum. I. L. Cohen*¹, T. R. Gomez¹, S. Y. Kim¹, B. Z. Karmel² and J. M. Gardner¹, (1)*New York State Institute for Basic Research in Developmental Disabilities*, (2)*NYS Institute for Basic Research in Developmental Disabilities*

Background:

Children with Autism Spectrum Disorder (ASD) display problems with socialization and show stereotyped movement patterns. We have clinically observed that such children often track the periphery of an unfamiliar room, and have seen similar behaviors in at-risk toddlers. While typically assessed with rating scales, social and repetitive behaviors also can be quantified with physical parameters (e.g., time spent in a target area, distance from target, speed of movement, etc) that can be automatically computed. Automated tracking has advantages over subjective ratings in terms of reliability and amount of information provided. It potentially is important for assisting with diagnosis, informing animal models of ASD, and providing objective measures of treatment intervention. However, its validity for ASD has not been examined.

Objectives:

To examine the degree to which automated tracking data correlate with rating scale measures of ASD.

Methods:

Children were observed during free play for 3 minutes before and 3 minutes after testing with the Autism Diagnostic Observation Scale – Generic (ADOS-G) in a large room (3.18 m by 4.85 m) with toys placed on the floor and table. The parent was seated in the northwest corner and asked to complete the Aberrant Behavior Checklist (ABC). NOLDUS Ethovision XT software provided X-Y coordinates of the child derived from a centrally-located ceiling-mounted camera.

To date, 19 observations from 18 children 3 to 14 years (mean (SD) = 7.2 (3.2) years) have been obtained. Diagnoses were: 14 ASD, 2 anxiety disorder, 1 ADHD; and 1 developmental delay.

Ratings (completed by parent) included: PDD Behavior Inventory (PDDBI); ABC (Sansone et al (2011) factors); parent interview with Vineland Adaptive Behavior Scales (VABS); and clinician ratings using Gotham et al (2007) scoring system for the ADOS-G. Ethovision measures included: mean distance (meters) from parent, from center of room, and from periphery (walls 90° and 180° away from parent); percent time near parent or periphery; speed (km/hour) of movement and rate of circling the room (responses/min). Correlation matrices were computed and $p < 0.05$ was adopted for this exploratory study.

Results:

The greater the distance from parent, the worse the scores for: PDDBI Sensory, Social Approach, Expressive Language, and Learning, Memory and Receptive Language; ABC Stereotypy and Social Withdrawal; ADOS-G Social Affect; and VABS Communication, Daily Living Skills, and Socialization domains (Pearson rs: 0.47-0.67).

The greater the time spent in periphery of room, the worse the scores for: PDDBI Sensory, Aggression, Social Approach, and Expressive Language Competence; ABC Social Unresponsiveness, Stereotypy, Hyperactivity, and Social Withdrawal; and VABS Communication,

Daily Living Skills, Socialization and Motor Skills domains (Pearson rs: 0.48-0.67).

The greater the rate of circling, the worse the scores for: PDDBI Sensory, Ritualisms, Social Pragmatic Problems, Arousal, Specific Fears, Aggression, and Social Approach; ABC Irritability, Social Unresponsiveness, Stereotypy, Hyperactivity, and Social Withdrawal; and VABS Motor Skills domains (Pearson rs: 0.46-0.77).

Conclusions:

These results are encouraging and suggest that automated tracking of social distance and repetitive behaviors yields valid information for assessing children with autism. We are collecting more data (including unaffected controls) to confirm these observations.

107.106 106 Early Assessment of Autism Spectrum Disorders: Correlation Between M-CHAT-R and ASD Diagnosis in a Portuguese Sample. C. C. Almeida^{*1}, A. Rodrigues² and D. L. Robins³, (1)*PIN - Progresso Infantil*, (2)*Faculdade Motricidade Humana*, (3)*Georgia State University*

Background: Autism Spectrum Disorders (ASD) screening is not yet a common procedure in pediatric settings in Portugal. In order to promote ASD screening, using a tool validated in other countries, one M-CHAT-R study has been started with the collaboration with Georgia State University; preliminary findings are presented.

Objectives: This study proposes to correlate M-CHAT-R scores with outcomes of diagnostic instruments used in ASD assessment, identify the more frequently reported items in the M-CHAT-R questionnaire, and evaluate the percentage of false negatives in a sample of toddlers diagnosed with ASD.

Methods: Parents of children referred for early interventions services completed the M-CHAT-R questionnaire before they started their children assessment ($n=31$). Their ages were between 20 and 30 months ($m=24.90$, $SD=2.96$). All the children in this sample completed an evaluation using ADOS, ADI-R and Griffiths Mental Development Scale and they were all diagnosed with ASD.

Results: Total M-CHAT-R results were significantly related to ADI-R Reciprocal Social Interaction score ($r=.856, p<.001$) and ADI-R Communication score ($r=.642, p<.001$), but not Restricted, Repetitive Behaviors ($p>.207$). Analyzing ADOS scores, a significant relationship was found between total M-CHAT-R score and ADOS Communication score ($r=.698, p<.001$), Reciprocal Social Interaction score ($r=.730, p<.001$), Play score ($r=.731, p<.001$) and Stereotyped Behaviors and Restricted Interests score ($r=.581, p<.001$). Item analysis of M-CHAT-R results also highlighted 4 items pertaining to pointing and joint attention that were failed by more than 83% of the children with ASD. Finally, 96.8% of the sample screened positive on the M-CHAT-R, meaning that just 3.2% were a false negative.

Conclusions: Results suggest that M-CHAT-R is a good instrument for identifying early symptoms of autism, indicated by the strong correlations with scores from ASD diagnostic instruments. Although is was not used as a screening tool, the small percentage of false negatives indicates that most of the children with ASD will present a positive M-CHAT-R and the higher the total M-CHAT-R score is, the more severe the ASD symptoms will probably be. The study will continue in order to get a larger sample and continue to reach more relevant conclusions for Portuguese context.

107.107 The Japanese Version of the Diagnostic Interview for Social and Communication Disorders 11: A Preliminary Study of Japanese Version. Y. Uno¹, T. Uchiyama^{*2}, T. Yoshikawa³, Y. Nakayama⁴, N. Ozaki⁵, J. Gould⁶ and L. Wing⁶, (1)*Yokohama Psycho-Developmental Clinic*, (2)*Fukushima University*, (3)*Aichi Prefectural Colony Central Hospital*, (4)*Tokyo Metropolitan Children's Medical Center*, (5)*Nagoya University Hospital*, (6)*National Autistic Society*

Background: The Diagnostic Interview for Social and Communication Disorders (DISCO) is a schedule for the diagnosis of autistic spectrum and related disorders and assessment of individual needs. The DISCO, which was developed by Wing and Gould, is widely used in Europe and Japan as a clinical and research instrument. Although it has been translated into Japanese, Swedish and Dutch, its reliability and validity have been studied only in U.K and Sweden.

Objectives: The purpose of this study is to examine the inter-rater reliability and the criterion-based validity of the Japanese version of the DISCO (DISCO-J). This is the first report on the DISCO-J.

Methods: The authorized Japanese translation of the eleventh version of the DISCO was used in interviews with parents of 22 children. 11 children had the diagnosis of Autism spectrum disorder (ASD) (89±22mths, M:F 8:3, mean IQ±SD 91.5±28.8) and 11 children were a sample with typical development (Age 75±23mths, M:F 3:8, IQ 102.8±14.1). One DISCO-licensed child psychiatrist carried out the interviews, rated all items of DISCO-J and made clinical diagnoses based on the classifications of pervasive developmental disorders in the Diagnostic and Statistical Manual 4th edition Text Revision (DSM-IV-TR). Another DISCO-licensed child psychiatrist observed the interviews, rated all items of DISCO-J and then made independent diagnoses based on the DSM-IV-TR. The inter-rater reliability of the assessments by the two psychiatrists using the DISCO-J and the criterion-based validity of the diagnoses using the DISCO-J and the DSM-IV-TR were examined.

Results: There was a significant difference between the results for sex ratio ($\chi^2=4.5, p=0.03$) but no difference was observed for age and IQ between the ASD group and Non-ASD group. For the inter-rater reliability, Cohen's kappa or intraclass correlation coefficient r was over 0.78 for all three sections of infancy, age of recognition / development and untypical behavior. For the diagnosis part, r was 0.88. For criterion based validity the concordance rate of DSM-DISCO diagnosis was 95% and κ was 0.91.

Conclusions: Based on this study, the DISCO-J appears to have good inter-rater reliability and criterion-based validity. Since these preliminary findings were for a small number of 22 subjects, it will be necessary to widen the study over a larger number of patients.

107.108 Sensory Features in Early Infancy Differ in High and Low Risk Infants. B. Hand^{*1}, R. L. Young², D. Robson², J. C. Heathcock¹ and A. E. Lane¹, (1)*The Ohio State University*, (2)*Flinders University of South Australia*

Background:

Reliable methods for the detection of autism prior to age 2 are lacking, preventing access for at-risk infants to efficacious early intervention. Analysis of differences in responses to sensation between typically developing infants and infants who later develop or are at-risk for autism has been proposed as one way of identifying risk for autism at earlier ages. Previous studies examining sensory differences between young children who are later diagnosed with autism and those who are not have been mixed in the literature. The variability of results in the literature regarding sensory behaviors as an early sign of autism makes it an area of interest for further research and exploration.

Objectives: The objective of this study was to evaluate whether infants aged 2, 4 and 6 months at high risk for autism differed in responses to touch and sound stimulation and mouthing behavior from infants not at risk for autism.

Methods:

A high-risk group (HR, n=24) contained participants with an older sibling or first cousin with autism and a second group included participants with no known family history of autism (LR, n=15). Participants were involved in a larger longitudinal study examining early signs of autism. Infants were assessed at regular time intervals from 2-18 months of age. For the purposes of this study, we evaluated sensory behavior in the first 6 months of life only. Videos of infants at ages 2, 4 and 6 months performing developmental assessments were coded for mouthing and responses to touch and sound stimuli. Video footage was standardized and only time that the infant spent in supine was evaluated for mouthing and touch. Time spent in supine and seated positions was evaluated for sound stimuli. Mouthing duration and frequency was recorded with minimum threshold duration of two seconds. Responses to touch and sound stimuli were evaluated utilizing a standardized coding protocol that captured orientation, startle, aversive, seeking, or appropriate responses. Videos were coded by two independent raters and inter-rater reliability of at least 90% was achieved at each time point. Data was analyzed visually using frequency plots comparing HR and LR on each

variable and each time point. Variables of interest were further explored using chi-square analysis.

Results: Preliminary results reveal significant differences between groups at 2 months of age on the likelihood of responding typically to unexpected sound in supine ($\chi^2= 4.95$, $p<.05$, $df=1$) and atypically to unexpected sound in supine ($\chi^2= 4.29$, $p<.05$, $df=1$), with HR subjects more likely to respond atypically. A non-significant trend indicated that the HR group was more likely not to mouth than the LR group at 4 months ($\chi^2= 3.07$, $p>.05$, $df=1$) and indicated a delayed trajectory of mouthing development between 2-6 months on visual inspection. No differences in response to touch were noted between HR and LR groups at any time point.

Conclusions: These results indicate that further investigation of early mouthing behavior and response to unexpected sound may reveal new early markers of autism that would improve efforts towards earlier identification.

107.109 109 Using the Autism Quotient and Empathy Quotient to Aid Diagnosis in Adults: Performance in a 'Real World' Clinical Setting. N. Gillan^{*1}, C. E. Wilson², L. O'Rourke¹, C. M. Murphy³, H. L. Hayward⁴, V. D'Almeida³, M. Gudbrandsen⁴, E. Daly⁵, C. Ecker⁵, D. Robertson³ and D. G. Murphy⁶, (1)King's College London, (2)King's College, London, (3)King's College London, Institute of Psychiatry, (4)Institute of Psychiatry, (5)King's College London, Institute of Psychiatry, (6)Institute of Psychiatry. King's College London

Background:

To date there have been few studies that examine screening and diagnostic instruments in adult populations referred for assessment of Autism Spectrum Disorder (ASD). The Autism Quotient (AQ) and Empathy Quotient (EQ) are designed for use in adult populations. It has been proposed that there are clinical advantages to using these instruments as they are less expensive and time consuming, and require less expertise to administer and interpret. However relatively little is known on how they perform in a 'real world' clinical setting

Objectives:

The aim of this study is to examine AQ and EQ scores in an adult clinical setting when compared to the outcome of ADOS and ADI..

Methods:

Diagnostic assessment for 57 adults (11 females, 46 males, mean age 31.05) were reviewed. The participants were referred to the Behavioural Genetics Clinic (BGC) in the Maudsley Hospital, South London and Maudsley Trust for an assessment of ASD. Each participant had completed the AQ and EQ before assessment, and completed ADOS and / or ADI and a clinical interview during assessment.

For each measure, participants were categorized as above or below threshold for ASD on the ADOS and ADI using the algorithm scores. A score of under 30 on the EQ and of over 30 on the AQ were taken to indicate an ASD positive score.

Results:

In this sample, 39 met ASD criteria on the ADOS and 36 met on the ADI.

Sensitivity and specificity was calculated in comparison with the ADOS. In this the AQ had a sensitivity of 71.42% and specificity of 50%. The EQ had a sensitivity of 70.97% and specificity of 12.5%. Using the EQ and AQ together had a sensitivity of 50% and specificity of 50%.

Sensitivity and specificity was calculated in comparison with the ADI. In this the AQ had a sensitivity of 85.71% and specificity of 60%. The EQ had a sensitivity of 79.31% and specificity of 42.86%. Using the EQ and AQ together had a sensitivity of 66.67% and specificity of 60%.

Chi squared was used to find which measure distinguished most accurately between ASD positive results on both the ADOS and ADI. The AQ was found to be a significant predictor of a positive ADI: $\chi^2(1, 26) = 4.75, p = .029$. No other results were significant.

Conclusions:

The AQ and EQ alone (at a threshold of 30) have relatively poor predictive power when used to aid diagnosis of ASD in adults within mainstream health care settings. We are currently investigating how using other thresholds on the AQ and EQ may improve performance.

107.110 110 Diagnosis of Autism Spectrum Disorders in a Global Clinical Drug Trial: Challenges and Solutions. J. E. Olson¹, F. K. Miller², S. R. Podolin³, K. A. Bertzos³ and C. A. Brady^{*3}, (1)*JOlson Consulting*, (2)*University of Michigan*, (3)*PharmaNet-i3*

Background: Clinical trials face critical challenges to ensuring rater competency and diagnostic accuracy. Challenges are magnified when diagnosing Autism Spectrum Disorders (ASD) because accurate diagnosis requires an astute understanding of the population and the ability to synthesize information from multiple sources. The phenotypic overlap between ASD and other psychiatric disorders is well documented. The Autism Diagnostic Interview – Revised (ADI-R) and Autism Diagnosis Observation Schedule (ADOS) have become the gold standard measures for classification of ASD with increased sensitivity and specificity. There are, however, challenges to their use in international clinical drug trials:

- Extensive training and demonstration of skill is required for use in research
- Ongoing training programs vary across the globe
- Cultural, ethnic and language-specific diversity
- No global centralized repository of trained clinicians

Objectives: 1) To train clinicians to use the ADI-R and ADOS in a global clinical drug trial; 2) Minimize variability in administration and scoring of these measures; 3) Meet required timelines and enrollment expectations; 4) Ensure that raters are able to accurately classify individuals with ASD; and 5) Design training for clinicians that, although time intensive, is manageable for a clinical trial setting.

Methods: Raters from 10 countries (Americas, Europe and Asia) participated in an ADI-R and ADOS training program for a clinical trial in

pediatric ASD. Rater experience, education and previous training documentation were evaluated against stringent criteria and prequalified raters were determined to fall into one of the following tiers:

1. Research reliable, with approved documentation
2. Experienced with the measure
3. Not experienced with the measures but approved to participate in training due to prior education and population experience

No additional training was required for research reliable clinicians ($n=19$ ADI-R; 17 ADOS). "Experienced" raters ($n=21$) were required to view and accurately rate the certification video(s) only and were not required to attend a 5 day rater training meeting (RTM). 116 approved raters trained on the ADI-R, ADOS or both measures at one of 7 RTMs. Training included 2.5 days each of ADI-R and ADOS training provided by research reliable trainers from the Autism Trainers Consortium. Following meetings each rater watched and scored the certification video, permitting tiered individualized training for this initially diverse group.

Results: Criteria for approval to rate in the trial included accurate classification by video. Preliminary data showed agreement in diagnostic classification for autism versus non-spectrum was excellent for both the ADI-R and ADOS.

Conclusions: International clinical trials in ASD face the challenge of accurately diagnosing subjects in a standardized way. The ADI-R and ADOS can be effectively and efficiently used by employing a modified training program combined with accurate assessment of previously trained clinicians. Efforts are being made to consolidate information about trained clinicians at all levels for use by researchers as a resource for future trials. The central location would also be a virtual workspace to share information about these measures to ensure a global standard for diagnosis of ASD in clinical drug trials.

107.111 111 The Utility of the BASC-2 Content Scales for Identifying Children and Adolescents with Autism

Spectrum Disorders. L. E. Bradstreet*, D. L. Robins and T. Z. King, *Georgia State University*

Background: The Behavioral Assessment System for Children, Second Edition (BASC-2; Reynolds & Kamphaus, 2004), is a comprehensive rating system that identifies adaptive and maladaptive patterns of behavior in school-aged children and adolescents. Profiles of scores on the BASC-2 clinical (e.g., Hyperactivity, Anxiety) and adaptive (e.g., Adaptability, Functional Communication) scales on the Parent Rating Scales are useful for differentiating between children with and without autism spectrum disorders (ASD). In addition to these scales, the BASC-2 also includes seven empirically and theoretically developed Content Scales representing underlying dimensional domains of clinically relevant behaviors: Anger Control, Bullying, Developmental Social Disorders, Emotional Self-Control, Executive Functioning, Negative Emotionality, and Resiliency. Currently, few studies have examined the utility of these scales for identifying children and adolescents with ASD (e.g., Volker et al., 2010).

Objectives: The purpose of this project is to test the hypothesis that the BASC-2 Content Scales will differentiate between school-aged children with and without ASD.

Methods: As part of a larger test battery, BASC-2 Parent Rating Scales were completed by the primary caregivers of 25 children and adolescents with ASD and 32 children and adolescents without ASD between the ages of 7-17 years old ($M = 12.3$, $SD = 2.6$). Diagnoses for individuals with ASD were confirmed by expert clinicians using the Autism Diagnostic Observation Schedule and the Autism Diagnostic Interview – Revised. All participants also received the Wechsler Abbreviated Scale of Intelligence. Initial analyses included independent samples t-tests to determine if mean scores on the BASC-2 Content Scales differ between the ASD and Control groups and chi-square tests to examine whether T-scores on Content Scales in the "Clinically Significant" range relate to diagnostic categorization of participants.

Results: No significant differences were found between the average Full Scale IQ scores in the ASD group ($M = 106.68$, $SD = 20.22$) and the Control group ($M = 107.16$, $SD = 13.91$), $t(40.72)$

= 0.10, $p = .92$. The ASD group showed significantly higher levels of problematic behaviors on all seven BASC-2 Content Scales compared to the Control group (all $ps < .002$). Additionally, there were significant associations between diagnostic group and the number of T-scores in the "Clinically Significant" range on Developmental Social Disorders $\chi^2(1, N = 57) = 21.66, p < .001$, Anger Control $\chi^2(1, N = 57) = 5.99, p < .05$, and Resiliency $\chi^2(1, N = 57) = 18.09, p < .001$. The ASD group had a higher number of clinically significant T-scores on these Content Scales than the Control group.

Conclusions: The present data indicate that the BASC-2 Content Scales successfully differentiate between children and adolescents with and without ASD. Specifically, clinically significant scores on the Developmental Social Disorders, Anger Control, and Resiliency Content Scales were associated with diagnostic group membership. This information is particularly relevant in the context of determining whether BASC-2 Content Scales could potentially provide useful screening information for ASD in settings where ASD-specific screening tools are not available or it is not feasible to administer several disorder-specific tools.

107.112 112 Comparisons of DSM-IV and DSM-5 Criteria for Diagnostic Outcomes When Used in Community-Based Teacch Centers. M. E. Van Bourgondien*, T. Dawkins and A. T. Meyer, *University of North Carolina*

Background: The recent controversy regarding proposed revisions to the diagnostic criteria for Autism Spectrum Disorder relates to concerns about the sensitivity and specificity of the DSM-5 criteria for identifying individuals who would meet criteria for autism by DSM-IV criteria. According to several reports, diagnostic sensitivity decreased by 30 to 40% whereby individuals who met criteria for a Pervasive Developmental Disorder on the basis of DSM-IV-TR criteria no longer met criteria for ASD in accordance with DSM-5 criteria (Gibbs et al., 2012; McPartland et al., 2012). However, diagnostic disagreement between the two systems has been observed in as few as 9% of individuals (Huerta et al., 2012). Most comparisons of DSM-IV and DSM-5 criteria have been conducted through retrospective analysis of the archival data of individuals previously diagnosed with an ASD. Community based prospective studies in which clinicians

concurrently assess individuals with both DSM-IV and DSM-5 criteria are necessary in order to further examine the sensitivity and specificity of DSM-5 diagnostic criteria for ASD.

Objectives: To conduct a prospective comparison of diagnostic conclusions using DSM-IV and DSM-5 criteria within a clinic setting.

Methods: All participants were seen for diagnostic evaluation at the University of North Carolina TEACCH Autism Program across multiple centers in North Carolina. Assessments included administration of the Autism Diagnostic Observation Schedule-2 (ADOS-2), the Childhood Autism Rating Scale-2 (CARS-2), and a developmental history interview. Diagnostic conclusions were made on the basis of the direct assessment and observation, developmental history, DSM-IV-TR criteria and on the basis of clinical judgment. In addition, clinicians rated participants on DSM-5 criteria for ASD on the day of the diagnostic. Data collection is ongoing with an anticipated sample size of 150 participants by February 2013. Preliminary evidence was obtained for 14 participants. The participants are representative of a variety of socioeconomic and racial backgrounds from both rural and urban centers throughout the state. The TEACCH Center conducts diagnostic evaluation on all ages from toddlers through adults. The age range of the first 14 participants was 1.09 to 17.06 years (mean = 6.53 years; SD = 4.85).

Results: In preliminary data, 78.6% of the participants assessed received a diagnosis of ASD. All met criteria on both the proposed DSM-5 and DSM-IV criteria.

Conclusions: Preliminary findings show consistency across DSM-IV and DSM-5 diagnosis using a prospective sample suggesting that DSM-5 is not likely to result in fewer diagnoses.

107.113 113 Validation of the Autism Detection in Early Childhood (ADEC) As a Level 2 Screening Tool for Autistic Disorder. Y. H. Nah*¹, R. L. Young¹, N. Brewer² and G. Choimes¹, (1)*Flinders University*, (2)*Flinders University of South Australia*

Background:

The prevalence rate of Autistic Disorder (AD) alone is estimated to be as many as two to four out of every 1000 children. This rate is in stark contrast to previous prevalence rates of about 0.5/1000 during the early 1990s and about 1.2/1000 during the early 2000s. The significance of this increase is that clinicians and paediatricians are likely to see an increase in children presenting with AD in their practice settings and thus need sufficient tools and training to identify them. Screening for ASD is the first step to improve early identification of children who might be considered at risk of the disorder and in need of further assessment, intervention and services. There is a critical need for further research to develop and validate screening tools for ASD in young children referred for developmental difficulties. The Autism Detection in Early Childhood (ADEC) was developed as an effective screening tool for AD for children from 12 to 37 months old.

Objectives: To investigate the psychometric properties (reliability and construct, concurrent, diagnostic and predictive validity) of the ADEC. Specifically, to examine how well the ADEC classifies children with AD as compared to the ADOS, the ADI-R and clinical judgment based on DSM-IV. In addition, to examine the screening properties of the ADEC using receiver operating characteristic (ROC) curve analyses to identify sensitivity and specificity and to determine the optimal cut-off score.

Methods: Parents and health care professionals who were concerned that their child presented with possible risk of developing an ASD participated in this screening study and were assessed with a battery of tests (ADEC, ADOS, ADI-R, Mullen Scales and Vineland). The ADEC was administered independent from the diagnostic assessor and blind to the results of the diagnostic evaluation. Likewise, the diagnostic assessor who administered the ADOS and ADI-R was blind to the ADEC assessment result. A best estimate clinical (BEC) DSM-IV diagnosis was made by the first author using all available information and assessment results, with the exclusion of ADEC data, to generate independent diagnoses.

The resulting sample consisted of 72 children with a BEC DSM-IV diagnosis of AD, 14 children with PDD-NOS, 49 children with other developmental

disorders (ODD) (e.g. language and developmental delay) and 20 typically developing (TD) children aged between 12 to 37 months.

Results: Internal consistency was high. The ADEC scores are also reliable across examiners and across test-retest administrations. The findings supported the construct, concurrent, diagnostic and predictive validity of the ADEC. In addition, the ADEC's factor structures are found to be similar to the proposed DSM-5 criteria. The ADEC also has high sensitivity, specificity and predictive values using a cut-off score of 11 with the validation sample.

Conclusions: This study proposes the ADEC to be an effective Level 2 screening tool to identify children with AD ranging from 12 to 37 months old and has the potential to be established as an efficient, psychometrically valid and a reliably administered screening tool for infants with AD.

107.114 114 Clinical Use of the Infant-Toddler Social and Emotional Assessment in Autism Spectrum Disorder. E. Mottes*, F. Apicella, E. Conti, A. Cosenza, S. Maestro, A. Narzisi, R. Tancredi and F. Muratori, *University of Pisa – Stella Maris Scientific Institute*

Background:

Studies suggest that a diagnosis of ASD can be reliably made in the second year of life being relatively stable over time; at the same time ASD diagnosis of young children can be complex in reason of different presentations and a less specific symptomatology overlapping temperament difficulties, emotional dysregulation, regulatory and attentional problems, cognitive and language delay. As a consequence there is a need for tools to support the characterization and identification of young children with or suspected of an ASD.

Objectives:

To determine the capacity of the ITSEA in identifying toddlers with a diagnosis of ASD.

Methods:

ITSEA is a parental questionnaire performing a profile composed of 3 areas of Problems (Externalizing, Internalizing and Regulatory

processes) and an area of Competencies. Each area is composed by different subscales, and three global item clusters (Maladaptive; Social relatedness and Atypical behaviors) can be obtained. Specifically two out of three item clusters refer to typical autism symptomatology.

Forty subjects (mean age: 32,2 SD:4,4; males: 32, females: 8) were recruited at the ASD division of the Stella Maris Scientific Institute; inclusion criteria were: 1) age between 24 and 36 months; 2) a diagnosis of ASD according to DSM-IV criteria and confirmed by ADOS; 3) no associated medical or neurological illness.

Average scores were compared to the scores of the population of ASD subjects from the original ITSEA validation study.

Statistical comparison (T-test for independent groups) with a group of children with Regulation Disorders of Sensory Processing (REG) according to CD:0-3 was obtained.

Results:

Abnormal scores resulted in at least one subscale or cluster in 100% questionnaires. The comparison with the original ITSEA ASD group showed a similar profile. As expected clinical scores were obtained on Social Relatedness and Atypical Item Clusters even if with lower percentages in respect to ITSEA group (44% vs 88% and 53% vs 95%). Competence domain was globally involved in 87% of cases with higher clinical percentages in Attention, Imitation/Play, Empathy and Prosocial Peer Relation subscales. None of the Problems domains were globally abnormal, but a clinical score was found in the Depression/Withdrawal subscale within the Internalizing area (47% vs 70% of the original ITSEA) and higher percentages of abnormal scores resulted in the Aggression/Defiance component within Externalizing Problem and, within Dysregulation domain, in the Negative Emotionality subscale which is related to a temperamental component and to the difficulty in modulating negative emotional response. Higher percentages were found also in Eating subscale. In the comparison with REG group significant differences were found in the Competence Domain

($p < .05$), in the Withdrawal subscale ($p < .01$) and in the Atypical Item clusters ($p < .05$).

Conclusions:

The results of this preliminary clinical application suggests a good capacity of the ITSEA in identifying Toddlers with ASD providing a profile in which both specific ASD manifestations (Social Relatedness, Atypical Behaviours, Withdrawal) and a global competencies impairment, temperamental and regulatory components may be highlighted.

107.115 115 Age At ASD Diagnosis in the UK Has Not Reduced Over Recent Years: Evidence From a Large ASD Research Database. F. Warnell^{*1}, M. A. Johnson², P. Ramesh³, H. McConachie¹ and J. Parr⁴, (1)*Newcastle University*, (2)*Institute of Health and Society, Newcastle University*, (3)*Newcastle University*, (4)*Institute of Neuroscience, Newcastle University*

Background: Early diagnosis of ASD is desirable to help parents understand their child's neurodevelopment, give parents appropriate management advice as early as possible, and commence intervention strategies that may improve children's developmental progress. In recent years, clinical initiatives and publicity about ASD have improved UK ASD diagnostic services. However, to date, systematically collected recent UK data about the age at diagnosis of children with ASD have been lacking.

Objectives: 1. To identify whether age at ASD diagnosis has changed over recent years in the UK. 2. To explore the phenotypic factors associated with earlier diagnosis.

Methods: Data were available from the Autism Spectrum Database-UK (ASD-UK). ASD-UK is a research database to which families of children with ASD are recruited by more than fifty multidisciplinary UK child health teams. Data are collected about each child, and families can be contacted about UK ASD research projects. Analysis of gender, ASD characteristics, learning disability, and social deprivation scores has already shown that ASD-UK children are broadly representative of children with ASD in the UK (Warnell et al., in preparation).

Results: Data from 548 children with ASD aged 2-16 years were available (male:female ratio of 4:1). Three quarters of the ASD-UK children were diagnosed between 2007-2012. For those years, children's median ages at diagnosis were: 2007, 53 months; 2008, 48 months; 2009, 58 months; 2010, 52 months; 2011, 61 months; 2012, 61 months. Considering all ASD-UK children, 58% were diagnosed before age 5 years; one quarter of children received their diagnosis before age 3 years. Overall, the age at diagnosis of girls and boys was very similar. Controlling for language ability, SCQ scores were similar for children diagnosed before, and children diagnosed after 5 years (60 months). Children with a clinical diagnosis of 'autism' were more likely to be diagnosed earlier than children with 'ASD' or Asperger syndrome (Autism median age at diagnosis 42 months; ASD median 49.5 months; Asperger syndrome median 90 months).

Conclusions: In the UK, the median age at ASD diagnosis remains around age 5 years; many children received a later diagnosis. An 'Autism' diagnosis was associated with an earlier age at diagnosis, but gender and a number of other aspects of the ASD phenotype were not. These data have implications for both parents and clinical services, regarding advice and support for families, and access to early intervention.

107.116 116 DSM-5 Criteria Applied to Toddlers Diagnosed with ASD by DSM-IV-TR. D. T. Jashar*¹, L. A. Brennan¹, D. L. Robins², M. Barton¹ and D. A. Fein¹, (1)University of Connecticut, (2)Georgia State University

Background: The currently proposed DSM-5 diagnostic criteria for autism spectrum disorders (ASD) include substantial revisions. The most significant changes include combining the subcategories (Autistic Disorder, Asperger's Disorder, and PDD-NOS) into one dimensional category of ASD, combining the social and communication domains into one, and requiring two rather than one restrictive and repetitive behaviors (RRBs) (at DSM5.org). Because of strong evidence of the relationship between early diagnosis and intervention with more positive outcomes (Myers & Johnson, 2007), it is important to have diagnostic criteria that have adequate sensitivity for children under three years. Concerns have been raised about the proposed DSM-5 criteria's sensitivity for very

young children (Worley & Matson, 2012) since repetitive behaviors may not be manifest in this age group.

Objectives: In order to address concerns about sensitivity of the proposed criteria in toddlers, this current study examined if toddlers who received an ASD diagnosis under the DSM-IV criteria would maintain their diagnosis with the proposed DSM-5 criteria.

Methods: Children ($n=234$) between the ages of 16 and 30 months ($M=25.77$, $SD=4.58$) who were part of a multi-site study examining the sensitivity and specificity of the Modified Checklist for Autism in Toddlers (M-CHAT; Robins, Fein, & Barton, 1999) and who received an ASD diagnosis were included in the study. Parent report and direct observation measures included various editions of the ADI, the ADOS Module 1, DSM-IV-TR criteria, and the examiner's additional behavioral observations. Items in these measures that reflected the proposed DSM-5 criteria were used to create an algorithm to determine if participants who met the DSM-IV-TR diagnosis for an ASD also met the proposed DSM-5 criteria.

Results: Preliminary results suggested that 29% of toddlers who previously met an ASD diagnosis no longer did so with the new criteria; the majority of toddlers did not meet criteria B2 (routines, rituals, and/or inflexibility) and B3 (restrictive interests) in the proposed DSM-5 criteria. Relaxing criterion B by requiring one instead of two RRBs increased sensitivity; 17% of toddlers who previously met an ASD diagnosis no longer did so with the currently proposed DSM-5 criterion A and a relaxed criterion B (1 out of 4 RRBs). Under both systems, children with diagnoses of PDD-NOS disproportionately lost the diagnosis, compared to children with a diagnosis of Autistic Disorder.

Conclusions: Because of the significant implications of early detection and intervention of ASD on outcome, it is important that the proposed DSM-5 criteria reflect the presentation of ASD in toddlers. Requiring two RRBs may negatively impact the early detection of ASD because these behaviors are not as apparent in toddlers. Requiring one RRB instead of two would significantly increase sensitivity.

107.117 117 Studying the Continuum of Autistic Traits with Peripheral Biomarkers: Preliminary Evidence for Vasopressin, Oxytocin, and BDNF. N. Brondino*¹, E. Emanuele¹, B. Auyeung², L. Visai³, N. Bloise¹, S. Re¹, M. Rocchetti¹, M. Boso¹, F. Barale¹ and P. Politi¹, (1)University of Pavia, (2)University of Cambridge, (3)Salvatore Maugeri Foundation, IRCCS

Background: There is still a debate if behavioral symptoms should be considered dimensionally with disability lying at one extreme of the distribution of traits, or whether they should be categorically defined. Some evidence supports the notion that autistic symptoms and behaviors should be regarded as dimensional traits. Recently, autistic traits in healthy controls have been correlated with thinner cortex in the superior temporal gyrus. To date, there are no available data on potential biochemical correlates for the autism spectrum continuum. However, studies have reported altered levels of several biomarkers in Autism: in particular increased levels of brain-derived neurotrophic factor (BDNF) and arginine-vasopressin (AVP) have been observed in individuals with autism spectrum conditions (ASC). On the other hand, a disruption in the oxytocin (OXT) system resulting in lower plasma levels of this peptide has been reported in participants with Autism.

Objectives: The present study aimed to investigate the role of AVP, BDNF and OXT as potential biochemical correlates of subclinical autistic traits in a cohort of healthy young adults.

Methods: One hundred and twenty-three subjects (64 males, 59 females) were recruited who were between 20 and 37 years old (M=23.17, SD=3.97). All participants were screened by a senior psychiatrist to exclude the presence of psychiatric disorders. Participants completed the Autism Spectrum Quotient (AQ), a widely used measure for the identification of autistic traits in the general population. Blood samples were obtained from all participants at the same time of the day to allow for circadian variation. All women in the study were taking oral contraceptives and thus we considered their sexual hormone levels as stable. Analyses were conducted using commercially available ELISA kits (R&D Systems, Minneapolis, MN) according to the manufacturer's instruction.

Results: We conducted a multiple regression analysis using the AQ score as the dependent variable and sex, vasopressin, oxytocin and BDNF levels as the independent variables. The model was significant ($p < 0.01$), explaining the 46% of the variance of the AQ score. Among the parameters included in the analysis, vasopressin levels ($p = 0.01$) and BDNF levels ($p < 0.006$) were independent predictors of AQ score.

Conclusions: The association between a gradient of autistic traits and AVP, BDNF and OXT levels in healthy adults and patients with autism will be discussed. These preliminary results support the hypothesis of a continuum underlying autistic traits in the general population.

107.118 118 Diagnostic Stability and Developmental Profiles of Autism in Preschool Age. E. Santocchi*¹, M. Prosperi¹, R. Tancredi¹, S. Baldini², R. Iglizzi¹, F. Apicella¹, A. Narzisi¹ and F. Muratori¹, (1)University of Pisa – Stella Maris Scientific Institute, (2)Stella Maris Scientific Institute

Background: In Autism Spectrum Disorders (ASDs) longitudinal studies show a wide range of outcomes in adaptive behavior domains (Bolte and Poustka, 2002), degree of autism (Jonsdottir et al., 2006; Szatmari et al., 2003), speech (Eaves and Ho, 1996; Turner et al., 2006), and IQ (Eaves and Ho, 1996; Szatmari et al., 2003); diagnostic stability of autism ranged from 81 and 87,5% (Moore e Goodson, 2003; Eaves e Ho, 2004). In the field of ASDs, diagnostic instruments have been helpful in defining population (Beglinger, 2001), merging samples (Lord, 2006), and comparing results across studies (Risi, 2006; Gotham, 2008). Recently, Gotham et al. (2009) published calibrated severity scores for the Autism Diagnostic Observation Schedule (ADOS; Lord et al. 1999). Developing these calibrated severity scores was inspired by the need in clinical practice and research for describing the severity of the behavior of children with ASDs referring to the core symptoms in the autism spectrum to try to delineate different outcome profiles.

Objectives: investigating the stability of autism diagnosis in preschoolers; describing developmental profiles of autism at preschool age; defining factors and predictive indexes of different developmental profiles.

Methods: the study has been conducted on 60 subjects who have received a clinical diagnosis of Autistic Disorder (AD; 20, 33, 3%) or PDD-NOS (40, 66,67%) at 36 months (Time 0; SD: 6,57; range 23-48) and who were re-assessed two years later (Time 1; mean: 61 months, SD: 7,75; range 47-78). The subjects were evaluated at T0 and at T1 with ADOS-G, revised diagnostic algorithms (Gotham et al,2007),the Calibrated Severity Scores (CSS; Gotham et al,2009) and psychometric tests.

Results: the FU has shown 5 different developmental profiles with regard to the clinical diagnosis received at T0 and at T1. Most children (17/20) diagnosed with autistic disorder at the age of 3, are going to keep the same diagnosis at the age of 5; some of these same children (3/20) are going to receive instead a diagnosis of PDD-NOS. None of them will exit autism. Among children diagnosed with PDD-NOS at the age of 3,in subjects who go out of autism at the age of 5 (9/40), CSS at T0 is significantly lower than in subjects who are diagnosed with AD at the age of 5 (12/40). The cognitive level (non verbal IQ - nvIQ) at 3 years is not different in the AD and in the PDD-NOS developmental profiles groups.

Conclusions: about 15% (9/60) of children early diagnosed as ASD exited the autism diagnosis at T1. CSS at the first evaluation could be hypothesized as a predictive factor of the outcome in ASD children, while nvIQ does not seem to be hypothesized as a predictive factor of the outcome. This preliminary statistical analysis is not sufficient to demonstrate the predictive value of these factors, since we should elaborate a regression model in order to confirm this correlation or to find further correlations among CSS,nvIQ and language level. Our aim is to collect further data on this sample and to study the developmental profiles of other subjects in order to confirm our preliminary results about factors and predictive indexes of the different developmental profiles of autism.

107.119 119 Using Mixed Methodology to Investigate ASD Diagnosis. A. O'Hare*¹, C. Catchpole¹, K. Forsyth¹, T. Johnson¹, I. McClure², K. McKenzie³, M. Rutherford², R. Rush¹ and A. Murray³, (1)*Queen Margaret University*, (2)*NHS Lothian*, (3)*University of Edinburgh*

Background: ASD assessment can be complex and time consuming, and research has indicated

that there can be wide variation in the age of diagnosis, with some individuals not receiving a diagnosis until later in childhood or even adulthood. The study presents information on the development of an evidence based methodology used, as part of a Scottish Government funded project, to identify the factors which may hinder or facilitate timely good quality diagnosis.

Objectives: To develop a consistent mixed methodology for data collection regarding the process of ASD diagnosis across the age span in Scotland.

Methods: Proportionate stratified sampling was used to identify a sample that was representative of the Scottish population. Part 1 of the project comprised a retrospective notes audit of 150 case notes and service interview of 8 child and 8 adult diagnostic services. In order to develop relevant factors, an Individual Data Collection Form and Service Configuration Tool were developed. The content was based on previous research, good practice guidelines, quality indicators and expert opinion. The evidence base was also examined to identify those factors which have been found previously to impact on: risk of ASD, referral for diagnosis of ASD and diagnosis of ASD. The tools were reviewed by practitioners with expertise in ASD assessment and piloted with case notes. Part 2 of the project involved focus groups with the same 16 services, during which the diagnosing professionals created local action plans focused on improving the capacity of their service and the robustness of their diagnostic process. These local action plans were aggregated into a national action plan.

Results:

The audit tools were found to:

- have good content, social and face validity;
- be easy to use in practice to gather relevant data.

The tools were used to gather data relating to:

- the diagnostic pathway for individuals;

- the summary diagnostic pathway for services;
- factors influencing waiting times for diagnosis for adults and children.

The focus groups:

- gave an effective opportunity for services to review and reflect on their performance;
- allowed comparison of diagnostic processes across Scotland;
- facilitated the development of local and national action plans for further improvement in ASD diagnosis.

Conclusions: The use of a mixed methods approach allowed for the collection of a rich detailed dataset pertaining to diagnosis of ASD, whilst also providing a useful method for services to reflect on their capacity and the robustness of their ASD diagnosis.

107.120 120 Adherence to Clinical Standards and Guidelines for ASD Diagnosis in Child and Adult Services in Scotland. I. McClure*¹, C. Catchpole², K. Forsyth², T. Johnson², K. McKenzie³, A. O'Hare², M. Rutherford¹, R. Rush² and A. Murray³, (1)*NHS Lothian*, (2)*Queen Margaret University*, (3)*University of Edinburgh*

Background: There is universal recognition of the importance of ensuring that the diagnostic process for ASD is robust and of high quality. This can be operationalised through the application of evidence based clinical standards and guidelines. A number of guidelines have been developed for use in the UK, including the SIGN guideline on ASD in children and young people (Scottish Intercollegiate Guidelines Network guideline 98; 2007) and the NICE guideline on ASD in adults (2012). In addition, The Scottish Government has produced its own Quality Diagnostic Standard (QDS) from expert consensus.

Objectives: To explore the extent to which ASD diagnostic services in Scotland adhered to the SIGN 98 and NICE Adult guidelines and the Quality Diagnostic Standard (QDS).

Methods: A mixed methodology was used: 16 representative ASD diagnostic services from across Scotland were randomly sampled, resulting

in an audit of 150 case notes; focus groups were then conducted with the same services. Clinical practice as evidenced within the case notes was mapped against the relevant standards and guidelines.

Results: Overall, child services were found to adhere to over 70% of SIGN 98 and the QDS. The adult services were found to adhere to over 50% of the NICE (Adult) guideline and the QDS. No significant relationship was found between adherence to either of the evidence based guidelines or the QDS and duration of the assessment process. The focus group participants identified ways to increase adherence to the guidelines and the QDS in the context of their local service, provided feedback and identified areas for future review.

Conclusions: There is variability within and between child and adult services across Scotland in adherence to the current clinical guidelines and QDS for the diagnosis of ASD. The outcomes of this study were used to help services improve the quality and robustness of their diagnostic procedures, and could also be used to inform future review of clinical guidelines and diagnostic standards.

107.121 121 An Action Plan for Improving Efficiency and Quality of the Process of ASD Diagnosis in Adults and Children. M. Rutherford*¹, C. Catchpole², K. Forsyth², T. Johnson², I. McClure¹, K. McKenzie³ and A. O'Hare², (1)*NHS Lothian*, (2)*Queen Margaret University*, (3)*University of Edinburgh*

Background: Delayed diagnosis is one of the main reasons for dissatisfaction with services expressed by families of individuals with ASD. However a challenge for ASD diagnostic services is to maintain a high quality and robust diagnostic standard whilst improving efficiency. This balance is reflected in a range of evidence based clinical guidelines and national targets, which services are expected to adhere to.

Objectives: To explore ways to improve the efficiency and quality of ASD diagnostic processes with local services to inform a national action plan.

Methods: Following a retrospective audit of 150 case notes from 16 Scottish ASD diagnostic

services, focus groups were conducted with the diagnosing professionals in each team. The results of the notes audit were used to inform the content of the focus group discussion. This centred around challenges and solutions related to improving the efficiency and quality of the ASD diagnostic process. Local action plans were generated, which were subsequently aggregated to form a national action plan.

Results: The key themes generated by the services which formed the national action plan were:

- Educating and informing referrers, multi-agency partners and families
- Having structured processes for requesting and gathering relevant contextual information
- Continuing professional development and training for diagnosing staff
- Having dedicated multi-disciplinary time for assessment and diagnosis of ASD
- Using time constructively with clear tools and processes at each stage
- Having clear pathways and good administrative processes

Conclusions: The mixed methodology provided an effective means of identifying challenges and solutions to achieving the balance between service efficiency and quality. The methodology and results from this research may be used to inform service structure in other countries.

107.122 122 Using the Child Behavior Checklist (CBCL) for Identification of Toddlers with Autism Spectrum Disorders. A. Narzisi^{*1}, S. Calderoni², E. Mottes³, S. Maestro³ and F. Muratori³, (1)University of Pisa - Stella Maris Scientific Institute, (2)Magnetic Resonance Laboratory, Division of Child Neurology and Psychiatry University of Pisa; Stella Maris Scientific Institute, (3)University of Pisa – Stella Maris Scientific Institute

Background:

The diagnosis of ASD can be reliably made by the second year of age, the American Academy of

Pediatrics recommends routine screening for autism risk at their 18- and 24-month well-baby visits. In fact, screening can offers the opportunity to alert primary care providers for further clinical evaluation and eventually early intervention. Instruments appropriate that evaluate the presence of autistic symptoms or the absence of socio-communicative skills in children who are at least 18 months are available. However, none of them has yet been found to be appropriate to detect ASD because of the high number of false positive or false negative cases.

Objectives:

To evaluate the sensitivity and specificity of the CBCL 1½-5 in the identification of children with Autism Spectrum Disorders (ASD), aged between 18 and 36 months.

Methods:

The CBCLs of 47 children with ASD were compared to the CBCLs of 47 toddlers with Other Psychiatric Disorders (OPDs) and the CBCLs of 47 toddlers with Typical Development (TD) in a case control study. One-way analysis of variance (ANOVA) and logistic regression with odds ratio (OR) analysis were performed. ROC analysis were performed in order to establish the optimal threshold that discriminate children with ASD from children with OPDs and TD.

Results:

One-way ANOVA revealed significant differences between the three groups. Logistic regression analysis showed that the Withdrawn and the Pervasive Developmental problems (PDPs) subscales can differentiate children with ASD from both children with TD ($P < .001$) and OPDs ($P < .001$). ROC analysis showed very high sensitivity and specificity for the PDP (0.98 and 0.91) and Withdrawn (0.92 and 0.97) subscales when ASD was compared to TD. Sensitivity and Specificity of Withdrawn (0.90 and 0.83) and PDP (0.85 and 0.83) remained high when comparing ASD vs OPDs.

Conclusions:

The CBCL 1½-5 seem to be able to differentiate children already diagnosed with ASD from children with TD and OPDs. The high sensitivity and specificity suggest to test this broadband tool in a screening survey.

107.123 123 Optimization of an Eye-Tracking-Based Categorical Screener for Autism Spectrum Disorders in 18- to 42-Month-Old Children. M. Ly*, M. Valente, A. Klin and W. Jones, *Marcus Autism Center, Children's Healthcare of Atlanta & Emory University School of Medicine*

Background: The overarching goal of this project is to develop performance-based measures that can be used as quantitative diagnostic screeners for autism spectrum disorders (ASD). This research stems from past work in which eye-tracking technology was used to measure spontaneous visual fixations during viewing of naturalistic social situations. While watching scenes of social interaction, toddlers with autism spent—relative to age- and verbal IQ-matched typically-developing (TD) controls—markedly increased time fixated on mouth, body, and object regions and markedly less time fixated on the eyes. While these measures showed robust between-group differences, subsequent research identified measures of dynamic visual scanning (moment-by-moment variation in looking patterns) that distinguished the ASD from TD groups with still larger effect sizes. These results, however, looked at group comparisons, and not at classification of individual children. In parallel to the current study, we are assessing the validity of visual scanning measures as a categorical screener for ASD in individual children between 18 and 42 months of age (Valente, Ly, Klin, & Jones). The current study aims to optimize the sensitivity and specificity of that screener by constraining the heterogeneity of the training set.

Objectives: The objective of this study is to test whether constraining the training sample for the initial ASD comparison group will improve the performance of an eye-tracking-based, categorical screener for ASD.

Methods: Eye-tracking data were collected while 50 toddlers, aged 18 to 42 months, viewed dynamic scenes of other children at play. Standardized clinical assessment measures (ADOS, ADI, cognitive, and language testing) confirmed diagnostic status for ASD and TD

children. Rather than using consecutive referrals to identify training and test samples, we selected the ASD training sample (ASD-1, N=50) on the basis of autism severity (focusing on children with lower severity scores). Relative to TD children (N=50), these children provided a training set with which to develop a model of expected differences between ASD and TD visual scanning. We then tested the remaining ASD children (ASD-2, N=50) as an external validation sample. Receiver operating characteristic (ROC) curves were created to analyze sensitivity and specificity.

Results: Preliminary results indicate that use of the constrained training sample decreased sensitivity but increased specificity of classification. Children in the validation sample were classified with sensitivity of 80% and specificity of 84%. These results are above recommended benchmarks for Level 1 developmental screeners.

Conclusions: By constraining the ASD sample to those with lower severity scores, the specificity in classifying individual children increased. In ongoing analyses, we are now measuring the extent to which additional approaches to optimization (time- and event-based, as well as cohort-based) will improve the classification. These analyses will test the viability of using differences in visual scanning as a categorical screener for autism spectrum disorders.

107.124 124 Developing the InCLEN Appropriateness Criteria for Autism Spectrum Disorder (INAC-ASD) and Attention Deficit Hyperactivity Disorder (INAC-ADHD). M. Nair*¹, S. Gulati², V. B. Deshmukh³, A. Mohapatra³, V. K. Bhutani⁴, D. H. Silberberg⁵, N. K. Arora³ and I. Group⁶, (1)*Medical College*, (2)*All India Institute of Medical Sciences*, (3)*The INCLEN Trust International*, (4)*Stanford University School of Medicine and Lucile Packard Children's Hospital*, (5)*University of Pennsylvania Medical Center*, (6)*The INCLEN NDD Study Group, The INCLEN Trust International*

Background: Autism [Pervasive Developmental Disorder (PDD) or Autism Spectrum disorder (ASD)] and Attention Deficit/Hyperactivity Disorder (ADHD) have been widely recognized for many decades. Yet there are no socio culturally appropriate diagnostic criteria available, as the construct continue to evolve.

Objectives: This study aimed to develop and validate appropriateness criteria for Autism Spectrum Disorders (ASD) and ADHD that can be applied in resource constraint environment.

Methods: An international multidisciplinary group of experts met at two face-to-face consensus meetings and reviewed the appropriateness of the current definitions as well as diagnostic criteria in the Indian context and developed the INCLIN Appropriateness Criteria: Autism Spectrum Disorder (INAC-ASD) and INCLIN Appropriateness Criteria -Attention Deficit Hyperactivity Disorder (INAC-ADHD). The INAC-ASD and INAC-ADHD criteria were based on DSM-IV-TR. The study was conducted on children aged 2-9 years by systematic random selection at the general pediatrics out-patient clinics of four tertiary care pediatric facilities. The selected subjects were administered the survey tool-kits by trained psychologists and their performance compared to other widely used tool [Childhood autism rating scale (CARS) for ASD and Conner's for (ADHD)] and validated through independent testing by a team of expert child psychologists and pediatric neurologists (Team diagnosis). The team diagnosis was taken as the reference standard.

Results: The overall diagnostic accuracy for 'PDD group' [AUC=0.97 (95% CI=0.93-0.99), z=32.12; P=0.0001], and various accuracy parameters for diagnosing 'PDD group' and autism compared with the reference standard of DSM-IV-TR was high (Sn=98%, Sp=95%, PPV=91%, NPV=99%, +LR=20, -LR=0.02) and (Sn=90%, Sp=95%, PPV=90%, NPV=81%, +LR=10, -LR=0.05 respectively). The concordance rate between the INAC-ASD and DSM-IV-TR for 'PDD group' was 82.52% [Cohen's κ =0.89 (95%CI=0.82 to 0.97); P=0.001]. Similarly, concordance rate between the INAC-ADHD and DSM-IV-R diagnosis of ADHD was 71.82% [Cohen's κ =0.45 (95%CI=0.32 to 0.58); P=0.001]. The overall diagnostic accuracy for INAC-ADHD cut-off score of ≥ 8 [AUC=0.98 (95% CI=0.94-0.99), z=67.02; P=0.0001], and various diagnostic accuracy parameters for differentiating ADHD from those with other neuro-developmental disorders (Sn=87.7%, Sp=42.9%, PPV=58.1%, NPV=79.4%, +LR=1.5, -LR=0.28) and normal children (Sn=87.7%, Sp=97.2%, PPV=98.0%, NPV=83.3%, +LR=31.5, -LR=0.12) as compared with the reference standard of DSM-IV-TR was high. The internal

consistency of INAC-ASD and INAC ADHD was 0.96 and 0.91 respectively. The convergent validity with CARS ($r = 0.73$, $P = 0.001$) and divergent validity with Binet-Kamat Test of intelligence was ($r = -0.37$; $P = 0.004$) for INAC-ASD and the convergent validity with Conner's 3 Parents Scale was moderate ($r = 0.73$, $P = 0.001$) for INAC-ADHD.

Conclusions: With the appropriateness of the international criteria for ASD and ADHD being documented in India, INAC-ASD and INAC-ADHD, socio-culturally appropriate tools could be used by clinicians to provide a consistent diagnostic approach and researchers to develop as well as validate intervention measures in India and similar settings elsewhere in the world.

107.125 125 Development and Validation of Consensus Clinical Criteria Inclen Diagnostic Tool Kits for Neuro-Motor Impairment (INDT-NMI) and Epilepsy (INDT-EPI). S. Gulati¹, M. Nair², A. Mohapatra³, V. B. Deshmukh³, V. K. Bhutani⁴, D. H. Silberberg⁵, N. K. Arora³ and I. Group⁶, (1)All India Institute of Medical Sciences, (2)Medical College, (3)The INCLIN Trust International, (4)Stanford University School of Medicine and Lucile Packard Children's Hospital, (5)University of Pennsylvania Medical Center, (6)The INCLIN NDD Study Group, The INCLIN Trust International

Background: A structured, validated diagnostic instrument for identifying children with neuro-motor impairment and epilepsy was needed for easy and standardized assessment by the primary care physicians in resource constraint environments, and for collecting epidemiological information for decision makers and scientists.

Objectives: To validate diagnostic toolkits for Neuromotor Impairments (INDT-NMI) and Epilepsy (INDT-EPI) for use by the primary care physician.

Methods: For INDT-NMI, standardized instrument comprising three sections (Section 1: triage questions: to elicit information on developmental milestones, Section 2: observations: by the physician in terms of hand function, gait and muscle weakness, Section 3: neurological examination: for confirmation of neuromotor impairments) and in INDT-EPI, precision-based 10-question evaluation form was developed. The study was conducted on children aged 2-9 years

by systematic random selection at the general pediatrics out-patient clinics of three tertiary care pediatric facilities. The assessment of study subjects were done twice. In step-1 the INDT-NMI and INDT-EPI was administered by primary care graduate physician and in step-2 diagnosis established by consensus of two Pediatric Neurologists each with at least three years experience in diagnosis and management of children (team diagnosis). The team diagnosis was taken as the reference standard.

Results: A total of 454 children 2-9 years age (mean age 60.4 ± 1.1 months) in INDT-NMI and 514 children (mean age was 60.1 ± 1.0 months) in INDT-EPI were enrolled in the study. The diagnostic evaluation was adapted to the local vernacular language, required 15- 20 minutes in an office-setting and allowed for additional time for family counseling. The diagnostic tool-kit INDT-NMI demonstrated psychometric properties with sensitivity and specificity of 85.8% and 95.3 %, positive and negative predictive values of 94 % and 88.5 %, and positive and negative likelihood ratios of 18.25 and 0.15 respectively when compared to the expert evaluation. INDT-EPI was also observed to have good psychometric properties, with sensitivity and specificity of 85.6% and 93.5%, positive and negative predictive values of 88.5% and 91.7%, and positive and negative likelihood ratios of 13.2 and 0.15 respectively when compared to expert evaluation.

Conclusions: A validated structured and intuitive toolkit for point-of-care diagnosis (INDT-NMI) and (INDT-EPI) in children by primary care physicians has been developed and would promote early treatment and timely, targeted referrals for expert evaluation, particularly in resource constraint environments.

Brain Imaging Program

108 Brain Imaging - Functional

108.126 126 Cognitive Flexibility Applied to Emotional Stimuli in ASD: A Behavioural and fMRI Study. M. Gomot*¹, H. Clery¹, F. Bonnet-Brilhault², B. Wicker³ and P. Fonlupt⁴, (1)*INSERM U930*, (2)*UMR Inserm U930*, (3)*Institut de Neurosciences de la Timone*, (4)*INSERM U1028*

Background: Patients with Autism Spectrum Disorder (ASD) display difficulties in changing strategy during daily activities or adapting their perspective, especially during social interactions. However despite number of evidence of deficits in both socio-emotional processing and cognitive flexibility in ASD, the interactive effects of difficulties in these two domains remain unexplored.

Objectives: Our aim is to investigate this interaction by assessing behavioural and brain correlates of cognitive flexibility when applied to emotional stimuli.

Methods: Thirteen adults with ASD and 15 age-matched controls participated in an event-related fMRI paradigm using an emotional version of the Wisconsin Card Sorting Task (WCST). The cards presented were surrounded by a coloured frame and represented emotional faces. Participants have to match cards on one of three possible dimensions according to a non spoken rule: frame colour, face identity or facial emotion.

Results: Behavioural results revealed that compared to controls, patients succeeded in fewer categories, committed more perseverative errors when switching to Emotion matching, and displayed longer RT for Emotion and Identity conditions. fMRI results showed activity in the neural network typically recruited during WCST in both groups. However switching to a new rule lead to larger brain activity in ASD than controls in the anterior cingulate cortex, striatum, cerebellum and the frontal and orbito-frontal regions, together with lower activity in the temporal poles. Results are discussed according to the sorting rule.

Conclusions: Findings are consistent with the difficulties in processing socio-emotional stimuli in ASD and suggest that cognitive flexibility abilities are strongly modulated by the nature of the information to be processed.

108.127 127 Atypical Causal Influences Between Brain Regions in Children with Autism Spectrum Disorder. L. Q. Uddin*, K. Supekar, C. Lynch, M. Barth, S. Ryali and V. Menon, *Stanford University*

Background:

Autism spectrum disorders (ASD) are complex neurodevelopmental disorders affecting multiple brain systems. Effective connectivity is defined as the causal influence one neural system exerts over another, and can be used to quantitatively examine links underlying information processing dynamics in the brain. In typically developing (TD) children and adults, the right fronto-insular cortex (rFIC) is part of a salience network (SN) thought to mediate interactions between other large-scale brain networks supporting internally-oriented and social cognitive processes and externally-oriented goal-directed behaviors.

Objectives:

We aimed to characterize causal influences between the rFIC and other brain systems in children with ASD compared with TD children. Specifically, we sought to assess the causal influence of the rFIC on major nodes of the default mode network (DMN) and executive control network (ECN), two brain systems for internally-oriented and externally-oriented processing, respectively.

Methods:

Functional MRI data was collected from 7-12 year old children with ASD and age-, gender-, and IQ-matched groups of TD children across various cognitive states; 1) task-free resting state (n = 20 ASD/20 TD), 2) arithmetic processing (n = 15 ASD/15 TD), and 3) social attention (n = 12 ASD/12 TD). Causal interactions between key nodes of the SN, DMN, and ECN were examined and compared between groups for each cognitive state using multivariate Granger causal analysis. Network nodes were identified from a previous published study. We followed methods as described by Seth et al. to test for causal influences between regions of interest (ROIs). Those directed connections whose mean across subjects in the group was significantly different from the mean of the null (F-value) distribution were identified using a stringent threshold ($p < 0.01$, FDR corrected for multiple comparisons).

Results:

Across all cognitive states, for both TD and ASD groups, the rFIC was found to be a causal outflow

hub in that this region that had a high number of causal outflow connections and low number of causal inflow connections. We found atypical patterns of causal influences emanating from the rFIC in children with ASD both during resting and task states. In the resting state, there were greater causal influences from the rFIC to nodes of both the DMN (VMPFC) and CEN (rPPC) in TD children compared to children with ASD. There were greater causal interactions within the SN (rFIC-ACC) as well as atypical causal interactions between the CEN and SN (rDLPFC-ACC) in children with ASD compared to TD children. During performance of an arithmetic verification task, there were greater causal influences from rFIC to ACC in TD children compared to children with ASD. During performance of a social attention task, no group differences in causal connectivity were observed.

Conclusions:

The current results are in line with the hypothesis that aberrant effective connectivity of the rFIC and other key network nodes may contribute to the autistic phenotype.

108.128 128 Attention Orienting in Autism Spectrum Disorders: Brain Function and Connectivity. J. Fitzgerald^{*1}, J. McGrath¹, K. A. Johnson², H. Garavan³ and L. Gallagher¹, (1)Trinity College Dublin, (2)University of Melbourne, (3)University of Vermont

Background: Deficits in attention are consistently reported in Autism Spectrum Disorders (ASDs) and researchers suggest that the behavioural deficits characteristic of ASD may be due to an inability to orient attention to social stimuli. Spatial attention orienting is a cognitive process that facilitates the movement of attentional focus from one location to another in response to a stimulus. Attention orienting is considered important for socio-emotional development, learning and a crucial component of joint attention. Neuroimaging studies support the modulation of two interacting networks in attention orienting, the bilateral dorsal frontoparietal network or the dorsal attention network (DAN) responsible for cognitive selection of sensory stimuli and the right lateralised ventral frontoparietal system or the ventral attention network (VAN) which functions to direct attention to unattended relevant stimuli.

Objectives: This study aims to dissociate dorsal and ventral attention networks in an ASD population to determine if the cognitive selection of sensory information (DAN) and/or the function to direct attention to behaviourally relevant stimuli are impaired using functional MRI techniques.

Methods: 21 individuals with high functioning ASD and 21 age and IQ matched control participants performed a Posner style spatial attention paradigm consisting of four trial types; valid, invalid, neutral and cue-only. Reaction time (ms) to target appearance was used to measure behavioural performance. Functional MRI data was acquired in a 3Tesla MRI scanner. Preprocessing and analysis of the data was carried out using AFNI and FSL imaging software. First-level contrasts and second-level t-tests were performed to evaluate within and between groups differences. All data was corrected for multiple comparisons at $p < 0.05$.

Results: ANOVA revealed participants performed significantly better on valid trials than invalid and neutral trials, $p < 0.001$, however there was no significant difference in behavioural performance between groups, $p = 0.436$. A t-test of cue-only trial activation revealed a significant difference in the right superior frontal gyrus between the ASD and control group, $p < 0.05$. In the ASD group, a t-test of invalid-valid trials revealed significant activation in the left temporoparietal junction while in the control group, only right superior orbital gyral activation survived correction. A between group comparison of invalid-valid trial activation yielded significant group differences in the parietal, frontal and temporal regions, $p < 0.05$.

Conclusions: Isolation of the bilateral dorsal attention network was facilitated by the analysis of cue-only trials. Reduced activation observed in superior frontal regions suggests that individuals with ASD are impaired in the ability to process and select cognitive information. Comparison of invalid-valid or 'reorienting' trials enabled the investigation of the ventral attention network. While behavioural results indicate that the ASD group performed similarly to the control group, analysis of fMRI images revealed significant differences in a number of regions. Differences observed in frontoparietal regions may be an

indication that individuals with ASD use a compensatory mechanism in order to attend to behaviourally relevant stimuli similarly to controls. These observations are in keeping with the theory that functional connectivity may differ in individuals with ASD in comparison to typically developing individuals.

108.129 129 Brain Routes for Reading in ASD and Neurotypicals. R. L. Moseley*¹, F. Pulvermüller² and Y. Shtyrov¹, (1)*MRC Cognition and Brain Sciences Unit*, (2)*Free University*

Background: Reading utilises two neural pathways: the first (lexical) route visually mapping whole words to their lexical entry to retrieve meaning, the second (nonlexical) mechanically decoding words via general grapheme-phoneme conversion rules of the given language in order to construct its pronunciation. Whilst neurotypical readers typically employ the direct lexical route for reading familiar regular words, a pattern of poor reading comprehension plus precocity at mechanically 'sounding out' words ('hyperlexia') suggests the same may not be true of readers with autism spectrum disorders (ASD), who may utilise different pathways and who often seem to lack a 'default' semantic processing mode.

Objectives: We attempted to compare visual word processing of short, simple words between participants with an ASD and age- and IQ-matched controls.

Methods: MEG and EEG recordings were taken as participants passively read single words. Following preprocessing of combined MEG/EEG data, we explored the neuronal generators underlying electrophysiological and neuromagnetic activity with source analysis using high-resolution structural MRI scans from each participant. Results were confirmed in both an anatomically-defined and data-driven regions of interest (ROI) approach.

Results: The physiological data revealed preferential recruitment of temporal areas associated with the lexical route in control subjects. Though showing less activation than controls in temporal areas, ASD participants showed no preferential use of either route, but additional recruitment of the nonlexical route associated with a dorsal stream of activation in parietal areas and BA 44. Greater activation of this dorsal route in ASD occurred throughout the

epoch, from 70ms after word presentation to 450ms. In addition, analysis of semantic differences between experimental words revealed many category-specific semantic differences in the control group that were lacking in the ASC group, particularly in the earliest time-windows.

Conclusions: In contrast to controls who preferentially employed the lexical route, people with ASC appear to automatically decode even familiar words, showing recruitment of additional pathways and theoretical consistency with hyperlexia, a tendency to mechanically phonologically-decode language whilst, in previous literature. The lack of automatic category-specific differences between words with different meanings in the ASD group supports the suggestion that whilst semantic processing in autism may not be globally impaired, semantic information may not be automatically activated without explicit instruction.

108.130 130 Written Praise Activates Mesolimbic Reward Circuitry in Autism Spectrum Disorders. C. R. Damiano*¹, E. Hanna¹, K. Dunlap², D. Cockrell¹, J. Aloï¹, S. Miller¹, J. W. Bodfish³ and G. S. Dichter⁴, (1)University of North Carolina at Chapel Hill, (2)Duke University, (3)Vanderbilt University, (4)University of North Carolina

Background: Research addressing reward processing in autism has consistently found impaired motivation for social rewards. To further refine the social motivation theory of autism, the present study directly compared reward circuitry responses to different types of social rewards in individuals with autism spectrum disorders (ASDs).

Objectives: The primary aim of this study was to examine reward circuitry responses to different types of social rewards, in individuals with and without ASD.

Methods: This study included 16 adults with confirmed diagnoses of ASD and 15 age- and IQ-matched adults without ASD. Brain activation during the anticipation and receipt of rewards was assessed using functional magnetic resonance imaging (fMRI) in a 3T MRI scanner. In the scanner, participants completed a modified version of an incentive delay task which involved four different reward types: 1) monetary rewards that participants won for themselves, 2) monetary

rewards won for another, anonymous individual, 3) the presentation of smiling face images, and 4) the presentation of different statements of written praise (e.g., "You got it! Great Job!").

Results: Analyses directly comparing anticipatory responses to different reward types revealed that individuals with ASD did not show relatively greater activation in any striatal regions to any reward types. However, while the ASD group showed relatively decreased activation in striatal reward regions (i.e., nucleus accumbens, caudate, and putamen) during the anticipation of money won for themselves, money won for other individuals, and smiling faces, $p < .005$, there were no group differences in striatal activation to written praise. Further, analyses within the ASD group alone revealed that the written praise condition was associated with enhanced striatal activation (including bilateral nucleus accumbens activation) relative to monetary rewards for oneself, monetary rewards for another individual, and presentation of a smiling face, $p < .005$. Further analyses will consider responses during the outcome phase of the task and relations between neural activation and symptom presentation within the ASD group.

Conclusions: Individuals with ASD were found to show reduced striatal activation during the anticipation of several reward types, including monetary rewards for themselves and for others as well as the presentation of smiling faces. However, no group differences were found during the anticipation of written praise. These preliminary findings suggest that reward motivation for praise may be relatively spared in ASD. This result raises the possibility that behavioral interventions in ASD could be adapted to capitalize on this relative area of strength to more effectively motivate individuals with ASD in didactic contexts and in social interactions.

108.131 131 An fMRI Study of Multisensory Integration of Audiovisual Speech in Autism Spectrum Disorders: Effects of Temporal Synchrony. R. A. Stevenson*¹, M. Segers², S. M. Brown², J. M. Bebko², T. Woynarowski³, J. K. Siemann³, S. E. Greenberg³, S. Oczak² and M. T. Wallace³, (1)Vanderbilt University Medical Center, (2)York University, (3)Vanderbilt University

Background: Individuals with Autism Spectrum Disorders (ASD) exhibit atypical sensory processing in multiple sensory modalities (Iarocci,

2006), including deficits in combining information across different sensory modalities (i.e., multisensory integration). One of the strongest factors influencing multisensory integration is the temporal relationship between different sensory inputs. Recently, deficits in the realm of multisensory temporal processing have been shown in ASD (Foss-Feig, 2009; Kwakye, 2011) and appear to be differentially affected with speech stimuli (Bebko, 2006). The neural substrates for the temporal integration of both low-level (Stevenson, 2010) and speech-related audiovisual stimuli (Nath, 2012) appear to be centered on the cortex surrounding the posterior superior temporal sulcus (pSTS). In addition to its central role in multisensory temporal processes, the pSTS has also been shown to differ anatomically (Levitt, 2003) and functionally (Pelphrey, 2008) in studies with ASD participants.

Objectives: Investigate the role of pSTS in multisensory temporal integration in ASD via fMRI to address the following questions:

- 1) How does multisensory gain seen in BOLD activation patterns differ between ASD and typically-developing (TD) participants,
- 2) Does the level of multisensory integration differ between social and non-social sensory inputs or between linguistic and non-linguistic sensory inputs?

Methods: Individuals with and without ASD (N=10 per group, scanning ongoing), matched for age and cognitive abilities, underwent an fMRI scan while passively viewing auditory-only, visual-only, synchronous audiovisual and asynchronous audiovisual presentations with three types of stimuli: social-linguistic (speaker reading a passage of a story), social non-linguistic (speaker producing non-speech verbal noises), and non-social, non-linguistic stimuli (hand playing notes on a keyboard). Concurrent eye-tracking ensured participants attended to the stimuli. Whole-brain GLMs were performed, and a region-of-interest analysis localized pSTS via a conjunction analysis of activations to auditory- and visual-only presentations independently for each stimulus type. BOLD responses to synchronous and asynchronous audiovisual presentations were then extracted from these ROIs and compared within and across stimulus types and groups.

Results: Data from both groups show reduced peak BOLD activation in the pSTS in response to synchronous relative to asynchronous audiovisual presentations, likely reflecting an increase in processing efficiency associated with multisensory binding (Stevenson, 2010; 2011). In the TD group, responses with social-linguistic stimuli showed the greatest reduction in peak BOLD signal (17%) relative to non-social, non-linguistic stimuli (7%). In contrast, analyses to date of our ASD cohort showed less reduction with social-linguistic stimuli (12%) than with non-social, non-linguistic stimuli (26%). Thus, our TD group showed greater processing efficiency gains with audiovisual speech, whereas the ASD group showed greater gains with audiovisual non-speech stimuli.

Conclusions: These data suggest the behavioral instantiations of impaired multisensory temporal processing seen in previous studies (Bebko 2006, Foss-Feig 2009, Kwakye 2011) may be, at least in part, a result of atypical neural processing in pSTS, particularly the impairments specific to language. Interestingly, perceptual-feedback training focused on multisensory temporal processing has been shown to improve TD individuals' abilities to integrate audiovisual stimuli (Powers 2009) through neuro-plastic changes in the pSTS (Powers 2012) and as such may be a possible remediation tool.

108.132 132 Gamma-Band Deficits During Language Processing in Adults with Autism and First-Degree Relatives of Children with Autism: An MEG Study. L. B. Wilson^{*1}, E. Slason¹, B. E. Pasko¹, S. Hepburn² and D. C. Rojas¹, (1)University of Colorado Denver, Anschutz Medical Campus, (2)University of Colorado

Background: Language ability, specifically a deficit in phonological processing ability, has been proposed to be one of six core broad autism phenotypes. Deficits involving phonology have been observed in a significant subset (ranging from 24 to 77%) of children with autism and have been reported in studies of unaffected first-degree relatives. Despite this, no neuroimaging studies have investigated phonological processing in individuals with autism or their first-degree relatives.

Objectives: Magnetoencephalography (MEG) was utilized to investigate the neurobiology of phonological processing in adults with autism as

well as parents of individuals with autism. The aim of the present study was to examine the presence of phonological processing deficits in individuals with autism as well as unaffected first-degree relatives in order to provide evidence in favor of or against the inclusion of phonological processing deficits as a core broad autism phenotype (BAP) trait.

Methods: Sixteen parents of a child with autism, thirteen adults with autism and seventeen controls performed a phonological priming task while undergoing whole-cortex MEG. The task consisted of four prime-target word conditions including homophones (e.g., PAUSE-paws) and related stimuli. Primes were presented below perceptual threshold (i.e., 30ms). Subjects, who were not informed that stimuli consisted of word pairs, performed a lexical decision task (i.e., is it a word or a nonword?) on all lowercase targets.

Results: In our priming condition that placed heavier demands on phonological decoding skills, adults with autism exhibited reduced evoked gamma band activity relative to both parents and controls in the left supramarginal gyrus (SMG) centered around 200 ms post-stimulus onset. Adults with autism exhibited an additional later reduction in evoked gamma within the left superior temporal gyrus (STG) relative to controls, and an additional earlier reduction in induced gamma band activity relative to first-degree relatives in the left STG and SMG. Reductions in evoked gamma activity were also observed in adults with autism for unprimed relative to primed stimuli in the left SMG relative to the control group, but in the right STG relative to the parent group. No differences in gamma activity were observed between the parent and control groups.

Conclusions: These results are consistent with phonological processing deficits in individuals with autism. While not providing clear evidence for phonological processing deficits as a core BAP trait, the present study does provide evidence for alternate neural strategies during phonological processing in unaffected first-degree relatives. Furthermore, these alternate strategies were found to be related to gamma-band activity, abnormalities in which have been suggested to be a candidate endophenotype in autism. These results suggest the potential of future imaging investigations of phonological processing in

unaffected first-degree relatives of children with autism. In addition, the present results do provide both behavioral and functional imaging evidence for phonological impairments in individuals with autism that could have potential translational significance for language interventions in autism.

108.133 133 Neural Responses to Biological Motion in the First Year of Life: A Functional near-Infrared (fNIRS) Study Comparing Low- and High-Risk Infants. L. C. Anderson^{*1}, D. Z. Bolling¹, R. H. Bennett¹, S. K. Mitchell², K. A. Pelphrey² and M. D. Kaiser², (1)*Yale Child Study Center*, (2)*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 attention and engagement from birth. The posterior superior temporal sulcus (pSTS) is a key node in a network of brain regions involved in biological motion processing in typical children and adults and shows dysfunction in autism (Kaiser et al., 2010). At present, the early development of this neural system is not well understood. Functional near-infrared spectroscopy (fNIRS), which measures oxygenated (oxy-Hb) and deoxygenated hemoglobin concentrations in cortical brain regions, is ideally suited to measure correlates of brain activity in awake infants.

Objectives: fNIRS studies of biological motion processing in infants have been limited to a narrow age range of typically-developing infants (Lloyd-Fox et al., 2009, 2011). We are charting the typical development of the neural underpinnings of biological motion processing across the first year of life and attempting to determine at what age neural differences emerge in infants who go on to develop autism.

Methods: In this prospective, longitudinal study, infants at low and high risk for autism completed fNIRS experimental measures at 3, 6, 9, 12, and 18 months, with provisional diagnoses at 24 months and confirmatory diagnoses at 36 months. Infants were defined as "high-risk" if they had an older sibling diagnosed with autism. We monitored regional cerebral blood volume changes using a 24-channel NIRS apparatus over bilateral temporal regions to measure brain activity while infants viewed 10s video clips of PLDs of biological

and scrambled motion. Infants were video-recorded so that looking time could be assessed off-line, frame-by-frame. Preprocessing included low (0.7 Hz) and high-pass (0.01 Hz) filtering and exclusion of trials containing excessive motion and/or visual attention less than 75 percent.

Results: To date, participants include 8 low-risk (LR) infants and 8 high-risk (HR) infants, matched on age (LR: $M = 6.20$ months, $SD = 2.19$; HR: $M = 6.69$ months, $SD = 2.41$). We calculated changes in oxy-Hb in each channel for integrated blocks of biological and scrambled trials. We then averaged channels in the left and right hemispheres separately to obtain waveforms representing the infants' neural response to biological and scrambled motion in bilateral temporal regions. While low-risk infants differentiated robustly between biological and scrambled motion in the right temporal region between 5-12 seconds post-stimulus onset, high-risk infants showed no difference between conditions during this time window.

Conclusions: These findings suggest that the neural mechanisms for processing biological motion are present in the first 9 months of life in typical development and show dysfunction in infants at risk for autism by 9 months, prior to the onset of any clear behavioral indications of autism. Although statistically only a fraction of the high-risk 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.

108.134 134 Neural Correlates of Empathy for Social and Physical Pain in Autism. S. Krach*, I. Kamp-Becker, M. Blanke, L. Müller-Pinzler, J. Sommer, A. Jansen, K. Becker, T. Kircher, F. Bremmer, W. Einhäuser and F. M. Paulus, *Philipps-University Marburg*

Background:

Persons with the diagnosis of Autism Spectrum Disorder (ASD) are characterized by an impairment to predict their social interaction partners' behaviors by hypothesizing on their thoughts and feelings, i.e., by impaired mentalizing (Frith and Frith, 2003). It has remained unresolved, whether persons with the diagnosis of ASD can empathically share others' feeling states in an embodied manner (Bird et al.,

2010). In a previous study we showed that empathically sharing an awkward situation with an observed protagonist (e.g., a person slipping in the mud) and accordingly his or her experience of the social pain embarrassment, yields cortical activation in a network including the anterior insula (AI) and the dorsal anterior cingulate cortex (dACC) (Krach et al., 2011), a network coding the affective reaction during empathy for physical pain (Singer et al., 2004).

Objectives:

In the present study we aimed at identifying the neural substrates involved in processing others' social pain experiences and the corresponding vicarious emotional reaction of embarrassment in a group of persons with the diagnosis of ASD. We hypothesized the ASD group to exhibit diminished activation of the so-called pain matrix in response to such situations. Based on the strong implications of alexithymic traits in ASD (Bird et al. 2010), we predicted that the subjectively reported intensity of vicarious embarrassment experiences would be less correlated with neural activation in these regions in individuals with ASD compared to the control group (CG).

Methods:

Fifteen young men who matched the DSM IV criteria for ASD and who had a confirmed ICD-10 diagnosis of high-functioning ASD participated in the fMRI study. Stimuli consisted of validated sketches displaying protagonists during various forms of public norm violations in every-day life situations (Krach et al., 2011). Stimuli were presented for 12s, followed by a rating period to indicate the intensity of the vicarious embarrassment experience with button a press.

Results:

On the behavioural level, the ASD group and CG showed comparable vicarious embarrassment reactions. The results of the fMRI study yielded a more distributed engagement of the pain matrix and brain areas implicated in mentalizing in the CG as compared to ASD group. The parametric modulations indicated significantly stronger associations of hemodynamic responses with the subjectively reported intensity of vicarious

embarrassment experiences within the pain matrix in CG as contrasted to ASD.

Conclusions:

The present results show, for the first time, that persons with a diagnosis of ASD do indicate to experience empathy for another's social pain as demonstrated for vicarious embarrassment. The neuroimaging data indicates that although central components of the pain matrix are implicated in this social pain experience in ASD, neural-activation measures in these regions were not informed by the subjective indication of this emotion. Our results help explaining the heretofore finding that persons with high-functioning ASD are capable to behaviourally indicate feelings of social emotions such as embarrassment (potentially via explicit recall of learned social norms), while at the same time they display profound difficulties in resonating with others' emotional events (Bird et al., 2010).

108.135 135 Neural Responses to Familiar and Unfamiliar Faces in Infants At High Risk for ASD: A near-Infrared Spectroscopy Study. J. B. Wagner^{*1}, B. Keehn², S. L. Marshall², S. Fox², H. Tager-Flusberg³ and C. A. Nelson², (1)*Boston Children's Hospital/Harvard Medical School*, (2)*Boston Children's Hospital*, (3)*Boston University*

Background: Neuroimaging work has provided evidence of atypical brain activity in response to faces in individuals with autism spectrum disorder (ASD) as well as in their first-degree relatives. Prospective work examining infants with an older sibling with ASD provides an opportunity to look for early neural markers of atypical face processing, some of which might relate to the broader autism phenotype and others that might be predictive of later ASD outcome.

Objectives: The present work examined neural responding to familiar and unfamiliar faces in high- and low-risk infants using near-infrared spectroscopy (NIRS), a state-of-the-art optical imaging technique, to see how these responses might relate to the broader autism phenotype.

Methods: As part of a longitudinal study of infant siblings of children with ASD and typically-developing children, NIRS was used to measure hemodynamic responding in 9-month-olds while

they viewed 16s videos of their mother and a stranger displaying a neutral expression. A 24-channel Hitachi ETG-4000 NIRS system was used to record changes in oxyhemoglobin (oxyHb) and deoxyhemoglobin (deoxyHb) over frontal and right-temporal regions. Analyses focused on mean oxyHb and deoxyHb responses to mother and stranger in an 8s time window beginning 4s after stimulus onset. Thirteen low-risk control infants (LRC) and eight infants at high risk for ASD (HRA) contributed two or more artifact-free trials for mother and for stranger and were included in the present analyses.

Results: In examining oxyHb responses to mother and stranger over right lateral regions, analyses revealed a main effect of identity ($p = .04$), such that infants show greater (more positive) responses to mother ($M = .013 \text{ mm}^3/\text{mol}$) than stranger ($M = -.035 \text{ mm}^3/\text{mol}$), and a main effect of group ($p = .019$), such that LRC show greater responding ($M = .018 \text{ mm}^3/\text{mol}$) than HRA ($M = -.040 \text{ mm}^3/\text{mol}$). In frontal regions, a marginally significant interaction between identity and group was found for oxyHb responding ($p = .06$). When explored further, LRC infants showed significantly greater oxyHb responses to mother ($M = .042 \text{ mm}^3/\text{mol}$) than stranger ($M = -.025 \text{ mm}^3/\text{mol}$) in frontal regions ($p = .025$), while HRA showed no difference between mother ($M = -.020 \text{ mm}^3/\text{mol}$) and stranger ($M = -.010 \text{ mm}^3/\text{mol}$; $p = .70$).

When examining deoxyHb, frontal regions showed a main effect of identity ($p = .022$), with greater (more negative) deoxyHb responding to mother ($M = -.012 \text{ mm}^3/\text{mol}$) than stranger ($M = .018 \text{ mm}^3/\text{mol}$). DeoxyHb also showed a trend towards greater responding in LRC ($M = -.009 \text{ mm}^3/\text{mol}$) as compared to HRA ($M = .014 \text{ mm}^3/\text{mol}$) in the frontal region ($p = .1$). No main effects or interactions were found when for deoxyHb responding in right lateral regions.

Conclusions: By 9 months, hemodynamic responses to familiar and unfamiliar faces reveal evidence of atypicality in infants at high risk for ASD which might relate to the broader autism phenotype. These infants will be followed longitudinally, and future work will explore relations between these early neural measures of face processing and later ASD diagnosis.

108.136 136 Early Neural Activation During Emotional Face Processing in Children with Autism. R. Leung*, E. W. Pang, M. L. Smith and M. J. Taylor, *University of Toronto*

Background: Impaired social skills are a hallmark of Autism Spectrum Disorders (ASD). The ability to accurately perceive and interpret emotional faces is integral in successful social functioning. Our group has shown significant differences in neural activity associated with emotional face processing in adolescents with and without ASD. Examining neural activity during emotional face processing in a younger cohort using the same paradigm will determine when differences in neural activity during emotional face processing emerge during development.

Objectives: We examined neural responses associated with emotional face processing in children with and without ASD through the use of magnetoencephalography (MEG). We hypothesized that a distinct spatiotemporal profile of neural activity during emotional face processing would be seen in children with ASD relative to typically developing controls.

Methods: We have preliminary data on eight children with high-functioning ASD, determined by ADOS and ADI, (7M, M=9.4+1.2 years) and nine typically developing controls (8M, M=9.2+1.1 years). Participants completed an implicit emotional face processing task while in the MEG scanner. Emotional (happy or angry) or neutral faces were shown concurrently with a scrambled pattern (target), on either side of a central fixation cross. Children indicated the location of the target. Individual structural MRIs were acquired for co-registration with MEG data. To examine the time course of neural activation during emotional face processing, global field power (GFP) plots were generated for emotional and neutral faces. The children also completed two subtests of the WASI and the Affect Recognition subtest of the NEPSY-II.

Results: To angry and happy faces, GFP plots showed similar trends in neural activity between groups, with peaks at approximately 140ms and 180ms. Control children showed consistently greater overall amplitudes of neural activity relative to children with ASD. A different pattern was seen for neutral faces. GFP plots showed

greater activity in controls peaking at approximately 140ms but greater neural activity in children with ASD at a second peak at approximately 180ms. Further analyses will be conducted, on a larger cohort of 15 children per group. MANOVA showed no significant effects of group or emotion on response latencies. Independent sample t-test showed significant differences in performance on the Affect Recognition subtest, with children with ASD (N=5) scoring lower (M=9.8, SD=2.0) than controls (N=8, M=12.0, SD=1.2), $t(11)=2.5$, $p=.031$.

Conclusions: Our preliminary results indicate that while children with ASD respond at similar latencies to emotional faces compared to controls, the underlying neural activity shows differences early on (100ms), similar to our previous findings in adolescents with and without ASD. This suggests that neural differences underlying emotional face processing are present in children with ASD. Of particular interest was the reversed pattern of neural activity to neutral faces, with children with ASD showing greater overall activity relative to control children. This raises a caveat for studies that use neutral as an emotional baseline, especially in autism. That emotional face processing deficits exist in childhood is further supported by behavioural findings that children with ASD recognized facial affect more poorly than children without autism.

108.137 137 Increased Occipito-Frontal and Decreased Basal Ganglia Coupling During Reasoning in Autistics. I. Simard¹, I. Soulières² and T. A. Zeffiro³, (1)*Centre d'excellence en Troubles envahissants du développement de l'Université de Montréal (CETEDUM)*, (2)*University of Quebec in Montreal*, (3)*Neural Systems Group, Massachusetts General Hospital*

Background:

Studies of fluid reasoning have characterized the involvement of regions in both frontal and parietal cortex (Jung & Haier, 2007; Perfetti et al., 2008). Increasing reasoning complexity is associated with increasing activity in this network, particularly in prefrontal cortical areas (Kroger et al., 2002; Wendelken et al., 2007). In addition, autistics tend to have higher scores when assessed with Raven's Standard Progressive Matrices (RSPM) compared to Wechsler IQ tests, and to exhibit more occipital and less frontal activity than non-

autistics while solving RSPM problems (Soulieres et al., 2010). These findings suggest that inter-regional functional coupling may be atypical in autism during matrix reasoning.

Objectives:

Our goal was to determine how reasoning complexity modulates inter-regional coupling in autistics compared to non-autistics.

Methods:

15 autistics (2F, 13M) and 18 non-autistics (3F, 15M) solved RSPM problems during one self-paced fMRI scanning session (3mm cubic voxels, TR 2.7 s). The RSPM includes 60 fluid reasoning problems of progressively increasing difficulty. Each RSPM problem was presented as a 3x3 matrix with the final entry missing. Participants were instructed to take as much time as needed to select the correct answer from the eight choices provided. Problems were divided into figural, analytical, and complex analytical categories based on reasoning complexity. Psychophysiological interaction analysis was used to examine the effects of problem complexity on inter-regional coupling for three seed regions located in left superior parietal lobule, right inferior frontal gyrus, and left inferior occipital gyrus. Seeds were determined by identifying local maxima in occipital, parietal and frontal lobes using conjunctions of problem solving task-related activity in a combined autistic and non-autistic group.

Results:

While both autistics and non-autistics showed similar problem solving accuracy ($p = 0.54$), the autistics were responding faster (5350ms, $p = 0.01$). Non-autistics showed stronger coupling with respect to task complexity among: (1) all three seeds and the basal ganglia and (2) occipital and parietal seeds and the cingulate gyrus. Conversely, autistics showed stronger coupling than non-autistics for increasing complexity between the left inferior occipital gyrus and the left superior frontal gyrus.

Conclusions:

As reported in previous studies, non-autistic participants showed stronger basal ganglia coupling with the three seeds as task complexity increased, suggesting that autistics rely less on the basal ganglia than non-autistics for decision-making. Also, as task complexity increased, coupling between occipital and frontal cortex increased more strongly in autistics. This result may reflect an increased reliance by autistics on perceptual processes when engaged in matrix reasoning, consistent with a more prominent role for perceptual processing in multiple high level tasks for autistics (Mottron et al., 2012).

108.138 138 Alterations of the Theory of Mind Network in Adults with ASD. J. Suttrup^{*1}, H. Meffert², B. B. Sizoo³, J. A. C. J. Bastiaansen², N. Valchev², L. Cerliani¹, C. Keysers¹ and M. Thioux¹, (1)*Netherlands Institute for Neuroscience*, (2)*NeuroImaging Center Groningen*, (3)*Dimence*

Background: Deficits in solving Theory of Mind (ToM) tasks have been associated with social impairments in children with autism spectrum disorder (ASD) (Frith, 2001). However, high-functioning adults with ASD perform well on ToM tasks while noticeable social deficits remain (Frith, 2004). Thus, is the ToM brain network functioning neurotypically or do network alterations persist? The few existing imaging studies indicate network alterations but do not deliver consistent conclusions.

Objectives: The aim was to characterize the ToM network in high-functioning adults with ASD using an fMRI dataset obtained during a classical False-Belief/False-Photograph task (Saxe and Kanwisher, 2003) and multiple statistical techniques.

Methods: The participants (17 high-functioning ASD patients, 17 age/handedness-matched controls) read 24 short stories followed by a statement to be rated as true or false. Twelve statements required inferring someone's true or false belief (Belief), twelve were about the representation of the reality on a picture (Photo). Differences in network recruitment (Belief > Photo) and the relative contribution of the different ToM network nodes during mentalizing were assessed. Functional connectivity modulated by mentalizing was compared using a PPI analysis with a seed in the right temporoparietal junction (R-TPJ), which is specifically involved in reasoning

about false beliefs (Saxe and Wexler, 2005). The within-subject variability of ToM network node activations was analyzed as described in (Dinstein et al., 2010). A voxel-based morphometry (VBM) analysis was conducted to reveal regional grey matter differences using the Dartel algorithm.

Results: Both groups showed high task performances (about 90% correct), and activated all the ToM network nodes during mentalizing. Nevertheless, a different weighting of the nodes in the ToM network was observed. The increases of activity in R-TPJ and the right superior temporal sulcus (R-STS) were larger in controls, while activations in L-TPJ and precuneus were larger in the ASD group. A percent-signal-change analysis confirmed that the balance in the level of activity between the ToM areas was different between groups (group x area interaction). Outside the ToM network, the left inferior frontal gyrus (L-IFG) was hyper-active during mentalizing in the ASD group. Mentalizing strengthened the connectivity between R-TPJ and R-STS as well as L-TPJ in both groups, but the R-TPJ – L-TPJ and R-TPJ – L-IFG connectivity was enhanced in the ASD group. The within-subject variability in cerebral activity during mentalizing was not enlarged in the ASD group. Finally, the VBM analysis revealed decreased hippocampal and increased L-IFG volumes in ASD, in agreement with a recent meta-analysis (Via et al., 2011).

Conclusions: High-functioning adults with ASD perform well in this ToM task and all the nodes of the ToM network are recruited. However, there are differences in network weighting and connectivity that cannot be explained by within-subject variability and are possibly due to differences in network development.

108.139 139 Inhibition of Superior Temporal Sulcus Activity by Repetitive Transcranial Magnetic Stimulation: The Effects On Social Perception and Implications for Autism. A. Saitovitch*¹, T. Popa², D. Grévent¹, R. P. Calmon¹, S. Meunier², N. Chabane³, F. Brunelle¹, Y. Samson⁴, N. Boddaert¹ and M. Zilbovicius¹, (1)*INSERM Unity 1000, Necker Hospital*, (2)*University Pierre et Marie Curie, ICM - Pitié-Salpêtrière Hospital*, (3)*INSERM Unity 1000, Robert Debre Hospital*, (4)*Pitié-Salpêtrière Hospital*

Background: The superior temporal sulcus (STS) is known to be implicated in social perception and social cognition processes. Previous brain imaging

studies have suggested that abnormalities within the STS would be related to social impairments in autism. Anatomic-functional abnormalities of the STS occurring very early in brain development could be one of the first steps in the cascade of neuronal dysfunction in autism.

Objectives: We aimed to study the effects of controlled and non-invasive STS inhibition with rTMS (repetitive Transcranial Magnetic Stimulation) on social perception parameters in healthy young subjects.

Methods: Fifteen healthy subjects (mean age = 22,0 ± 2,5) were recruited for the study. All subjects underwent a structural MRI for a precise localization of the stimulation target for each individual. Subjects underwent both sham stimulation and inhibitory rTMS delivered over the right posterior STS (mean Talairach coordinates: 50 -53 15). Gaze parameters were measured with a Tobii-120 eye-tracker during passive visualization of social movies before and after each stimulation session. The eyes of the characters in each movie were selected as areas of interest to be analyzed. Eye-tracking data was processed with Tobii Studio® software. Data was submitted to a repeated ANOVA with corrections for multiple comparisons, with fixations to the eye-areas before and at several time-points after each stimulation as the repeated factor, and stimulation type as the between group factor.

Results: Repeated ANOVA showed a significant stimulation effect of the stimulation type on social perception parameter ($F_{(1, 14)} = 9,48; p = 0,008$). Post-hoc analysis showed a significant reduction of fixations to eyes-areas after rTMS, but not after Sham.

Conclusions: The results of our study show that STS activity can be modulated by a non-invasive painless procedure, such as rTMS, with significant behavioral effects on social perception. These results open up new perspectives on therapeutic strategies in autism.

108.140 140 Tempororo-Cerebellar Interactions Predict Mentalizing Ability in Youth with Autism: Fmri and DTI Evidence. A. Jack*¹ and J. P. Morris², (1)*Yale University*, (2)*University of Virginia*

Background: Posterior superior temporal sulcus is specialized for interpreting perceived human actions, and disruptions to this site have been documented in autism spectrum disorder (ASD). Previous work with typically developing adults has indicated that right posterior superior temporal sulcus (RpSTS) may be supported in its role in biological motion processing by interactions with left Crus I (LCrusI) of neocerebellum (Jack et al., 2011; Sokolov et al. 2010; Sokolov et al. 2012). We hypothesized that disordered RpSTS-LCrusI interactions could predict social deficits in ASD.

Objectives: Investigate relations among individual differences in 1) functional interactions between RpSTS and LCrusI, 2) temporal and cerebellar white matter, and 3) mentalizing ability among adolescents with ASD and typically developing comparison youth.

Methods: 15 high functioning adolescents (12-17 yr) with ASD and 15 same-age comparison youth participated in a simple manual imitation task conducted in the scanner. The format of this task, which involved both observation and imitation of a human hand pressing a randomized sequence of buttons, as well as execution of identical sequences of button presses using visuospatial cues in the absence of a human model, allowed for isolation of brain activity related to observation and use of human motion cues. White matter integrity for these youth was assessed using diffusion tensor imaging (DTI), and behavioral ratings of mentalizing ability were collected via parent report and lab-based assessment. We predicted that stronger interactions between RpSTS and LCrusI during processing and use of biological motion information, as assessed via psychophysiological interaction analysis (PPI), would be associated with better mentalizing ability. We also hypothesized that analysis of DTI data using Tract-Based Spatial Statistics would indicate that better mentalizing ability would be related to higher white matter integrity in cerebellar regions and in tracts theoretically relevant to RpSTS function (i.e. inferior and superior longitudinal fasciculi [ILF; SLF]).

Results: Our sample of high functioning adolescents with ASD and comparison youth did not differ on IQ, head motion, response time, or response accuracy. Consistent with our hypotheses, stronger RpSTS-LCrusI interactions

were associated with better mentalizing outcomes among teens with ASD. Lowered white matter integrity was observed in temporal ILF/SLF among youth with ASD; furthermore, individual differences in white matter integrity in this region were related to parent-reported mentalizing ability across the full sample, and these differences in temporal ILF/SLF also helped to predict the strength of RpSTS-LCrusI interactions during biological motion processing.

Conclusions: These results indicate that variability in neocerebellar interactions with key cortical social brain sites, and white matter integrity in temporal regions, may help explain individual differences in social perceptual outcomes in ASD.

108.141 141 Functional Neuroimaging Correlates of Intentional Biological Motion Processing in Unaffected Siblings of Children with ASD. A. A. Ahmed* and B. C. Vander Wyk, *Yale University*

Background: **A network of brain regions implicated in the processing of social stimuli has been investigated in typically developing children and those who have an autism spectrum disorder (ASD) to identify neural mechanisms of social behavior. Doing so improves our ability to use quantitative endophenotypes to characterize individuals beyond a categorical diagnosis. Moreover, investigating social brain activity in unaffected siblings of children with ASD could uncover brain mechanisms that compensate for inherited risk. For example, unaffected siblings showed unique patterns of brain activity in the right posterior superior temporal sulcus (pSTS) when they viewed point-light displays of human biological motion relative to scrambled motion. In action perception, neurotypical children and adults, but not children with ASD, showed preferential activation in the pSTS to human biological actions that are incongruent with a prior displayed intention (positive or negative emotion).**

Objectives: **To investigate the functional activation of social brain regions implicated in action perception in unaffected siblings of children with ASD, relative to typically developing children.**

Methods: Twenty-two unaffected siblings of children with ASD (age = 12.58, SD = 2.43) and a control group of twenty-two typically developing children who did not have a brother or sister with ASD (age = 11.63 years, SD = 1.85) were scanned on a Siemens 3T MRI scanner. The groups were matched on gender (8 females) and there were no significant differences in age or T-scores on the Social Responsiveness Scale (p = 0.15 and 0.29 respectively). Average SRS scores were below the threshold for mild ASD (49.36 for siblings, 45.55 for controls). All participants were shown a 6'16" paradigm consisting of a human actor who displayed positive or negative affect towards one of two cups on the screen. The actor then picked up one of the two cups in either a congruent or incongruent fashion. Congruent trials matched the displayed intention; the actor reached for the same cup if she displayed positive affect or the opposite cup if she displayed negative affect. Conversely, action did not match intention in the incongruent trials. An empirical region-of-interest in the right pSTS was created with an activation-likelihood estimation meta-analysis, in which published co-ordinates are used to create a probabilistic map of regions most likely to be active to a chosen class of stimuli. Waveforms from this region were extracted, and response was defined as activation at 10 seconds after stimulus onset relative to initial activation.

Results: Typically developing children were found to significantly differentiate incongruent and congruent actions in meta-analytically defined pSTS (paired $t(21) = -3.6802$, $p = 0.001392$), replicating previous findings. Unaffected siblings, however, did not differentiate the two conditions (paired $t(21) = 0.6162$, $p = 0.5444$).

Conclusions: These findings lend further evidence to the hypothesis that brain activations provide information that transcends diagnostic categories. Specifically, we show that unaffected siblings display atypical action perception processing despite showing typical levels of social cognitive behavior, as measured by the SRS. Understanding the neural mechanisms of

social cognition in siblings could shed light on the influences of genetic risk for ASD upon the brain.

108.142 142 The Influence of Social Valence On Imitation and Observation of Facial Expressions in Autism Spectrum Disorder. M. Schulte-Rüther*¹, A. Pohl¹, S. Krall¹, E. Oberwelland¹, G. R. Fink², B. Herpertz-Dahlmann¹ and K. Konrad³, (1)University Hospital Aachen, (2)University Hospital Cologne, (3)Research Center Jülich

Background:

It has been suggested that an early deficit in the human Mirror Neuron System (hMNS) is one of the key problems in autism spectrum disorder (ASD). Early dysfunctions related to the intuitive understanding and mental representation of actions and emotions may result in cascading deficits in social interaction. Alternatively, observed differences in brain activation within the hMNS may be a secondary effect, influenced by social motivation, attentional effects, and stimulus properties (such as emotional and social valence).

Objectives:

The present study aimed at investigating the hypothesis of a deficit in the hMNS in adolescents and young adults with ASD using functional magnetic resonance imaging (fMRI). Furthermore we aimed to explore whether activation in the hMNS and other regions associated with facial imitation and observation is modulated by the social valence of facial stimuli.

Methods:

We presented 15 patients with ASD and 18 typically developing controls (TDC), aged 12-20, with videos of facial expressions (smile or frown), which they should either imitate or merely observe. Video recordings of the participant's faces during the fMRI scan were used to ensure proper performance. Stimulus faces belonged to two groups differing with respect to social valence, representing either "friends" or "foes". Social valence was implicitly manipulated before the fMRI scan by means of a simple multi-round dictator game using the stimulus faces as co-players. They either generously gave points to the participants ("friends") or retained most of the

points for themselves ("foes"). All participants were able to make the distinction between "friends" and "foes" as reflected in their own performance during the game.

Results:

For both TDC and ASD subjects we observed significant activation in areas previously associated with the hMNS (right inferior frontal cortex, including pars opercularis, and right premotor cortex (BA 6)), as well as in the right amygdala and bilateral occipital cortex, extending into superior and inferior temporal cortex (conjunction analysis of observation and imitation versus baseline, $p < .05$ voxel-level, FWE-corrected for the whole brain). In the direct group comparison, no significant decrease in activation could be observed for ASD in areas associated with the hMNS, even at a very low threshold ($p < .05$ uncorrected, voxel level). In TDC we observed a significantly stronger modulation of brain activation by social valence in the right amygdala as compared to participants with ASD ($p < .05$ voxel level, FWE-corrected for ROI). In TDC, activation in this area was stronger for facial expressions which were congruent to the social valence of the stimuli (i.e. smiling "friends" and frowning "foes", $p < .05$ voxel level, FWE-corrected for ROI).

Conclusions:

Our results argue against a fundamental deficit of the hMNS in ASD. Irrespective of social valence, areas previously associated with the hMNS were activated during observation and imitation of videos with facial expressions. The modulation of amygdala activation by the social valence of stimulus faces suggests a role for the amygdala in detecting congruency of social valence and displayed emotion. This effect was absent in participants with ASD suggesting a lack of using social valence information in face-to-face situations.

108.143 143 Oscillatory Neural Responses to Speech and Nonspeech Sounds in a Nonverbal Child with Autism. S. Yau*¹ and J. Brock², (1)Macquarie Centre for Cognitive Science, (2)Macquarie University

Background: EEG and MEG are widely used in studies of auditory processing in Autism Spectrum

Disorders (ASD). However, for practical reasons, research has been restricted primarily to high-functioning children and adults and little is known about the neural processing of auditory stimuli in the most profoundly affected individuals. Within ASD, language skills vary widely. As a result of limited research in children with ASD without language, very little is known about the neural correlates of language in this population.

Objectives:

The current study used Magnetoencephalography (MEG) to investigate neural responses to speech and nonspeech stimuli in a nonverbal child with Autism.

Methods:

The case was a single 8-year-old autistic child, AA. AA was diagnosed with Autism on the Autism Diagnostic Observation Schedule (ADOS) and was below basal on the cognitive and language tests administered. AA is nonverbal and communicates via symbols on the iPad.

Brain responses to speech and nonspeech stimuli played binaurally were recorded using 160-channel MEG while the child watched a silent DVD. Speech stimuli were natural /a/ sounds, while nonspeech stimuli were complex tones consisting of sine waves that were carefully matched to the first three formants of /a/, and void of the fundamental frequency that gave it 'speechiness'. The child's brain responses were compared to those of 29 typically developing children and verbal autistic children (ages 7-13) undergoing the same procedures.

Results: AA showed a very clear and strong evoked response to nonspeech stimuli, compared to speech stimuli. This was reflected in strong increase in alpha (8-12Hz) and low beta (13-30Hz) power post-stimulus as well as alpha phase-locking in the left hemisphere. This pattern of results was not found in any of the typically developing children or verbal autistic children. In contrast, AA's brain responses to speech stimuli were hardly visible. Again, this was strikingly different to the other 29 participants.

Conclusions:

The present case study provides unique insight into the relationship between auditory processing in the brain and language impairment in children with ASD. Results from the main study involving 15 typically developing and 15 ASD children will also be presented, comparing individual differences in neuromagnetic responses to the degree and nature of language impairment (as measured on performance on tests of language and social communication).

108.144 144 Associations Between the EFHC2 Gene and Male Vulnerability to Impaired Social Cognition. C. M. Startin^{*1}, C. R. Gibbard¹, C. A. Clark¹ and D. H. Skuse², (1)*UCL Institute of Child Health*, (2)*Institute of Child Health, UCL*

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. Using Turner Syndrome (TS, X-monosomy) women to investigate genes on the X chromosome which affect social cognition we have identified an influence of SNP rs7055196 in the X-linked EFHC2 gene; women possessing the rare G allele (8.8%) showed poorer facial fear recognition than women possessing the common A allele. We have recently extended this work to neurotypical males (also X-monosomic), finding that G allele males also show poorer facial fear recognition accuracy than A allele males. Further, G allele males performed poorer on the Reading the Mind in the Eyes task (RMET) compared to A allele males; this is a theory of mind task which consists of a series of images of the eye region and participants are required to identify the mental state portrayed. ASD individuals also perform poorer and show differences in brain activity in regions of the social brain during the RMET compared to controls. This suggests there may be similarities between ASD males and neurotypical males possessing the rare G allele at SNP rs7055196 in terms of performance and neural activity during the RMET.

Objectives: We compared neural activity during a modified version of the RMET between high functioning ASD males and neurotypical males possessing the A and G alleles at SNP rs7055196.

Methods: Using an fMRI paradigm, we recorded neural activations of high functioning ASD males, neurotypical males possessing the A allele at SNP rs7055196 and neurotypical males possessing the G allele at SNP rs7055196 during a modified version of the RMET. This version of the task consisted of the original task along with a comparison task in which participants were asked to judge the age of the person in the images. The three groups were matched for age and IQ, and activations compared across groups.

Results: ASD males and neurotypical males possessing the rare G variant at SNP rs7055196 show similarities in neural activations of regions in the social brain during the modified RMET. In comparison, neural activations for both of these groups differ from those produced by neurotypical males possessing the common A allele at SNP rs7055196.

Conclusions: Our results suggest an association between theory of mind abilities and the EFHC2 gene. The location of this gene on the X chromosome supports a role for X-linked genes in contributing towards the sex difference in impaired social cognition, helping to explain why males are more vulnerable to ASDs compared to females. Further, this work suggests variation within the EFHC2 gene may contribute towards the development of autistic traits, and this gene is a prime candidate gene for further investigation into genetic contributions towards these traits.

108.145 145 Diagnostic Classification for Autism in Male Adults Based On Resting State fMRI Fractal Connectivity. M. V. Lombardo^{*1}, M. C. Lai¹, B. Chakrabarti², J. Suckling¹, M. R. C AIMS Consortium³, S. Baron-Cohen¹ and E. T. Bullmore¹, (1)*University of Cambridge*, (2)*University of Reading*, (3)*University of Cambridge, Institute of Psychiatry, University of Oxford*

Background: Much emphasis in autism research has been placed on systems-level atypical brain connectivity. Almost all published work thus far has measured 'functional connectivity' via Pearson's correlation coefficient or independent components analysis over a specific low-frequency band. Both do not take into account the long memory fractal properties that are inherent within BOLD fMRI time-series data. New measures are now available that account for such fractal properties, but it is an open question as to whether such measures of 'fractal' connectivity

are more sensitive than more conventional measures of 'functional' connectivity. Here, we investigate this question via testing the predictive utility of 'fractal' versus conventional measures of functional connectivity for making diagnostic predictions on adult males with and without autism.

Objectives: To assess the predictive utility of patterns of resting state 'fractal' connectivity and conventional measures of functional connectivity for diagnostic classification of adult males with and without autism.

Methods: Thirty neurotypical and thirty high-functioning adult males with a diagnosis of an autism spectrum condition (ASC), matched on age (18-45) and IQ, were scanned with fMRI at 3T (TR=1302 ms; 512 whole-brain volumes) while being instructed to stay awake and keep their eyes closed. BOLD time-series were extracted from 110 regions from a standard anatomy-based brain atlas and the mean time-series from each region was decomposed with a maximum overlap discrete wavelet transform. Conventional measures of 'functional' connectivity were computed using Pearson's correlation on wavelet scales 2 (0.096-0.192 Hz), 3 (0.048-0.096 Hz) and 4 (0.024-0.048 Hz). Long memory 'fractal' connectivity measures were estimated via asymptotic wavelet correlation matrices that measure convergence of the wavelet correlation spectrum on an asymptotic value across a range of low frequency scales (Achard, Bassett, Meyer-Lindenberg, & Bullmore, 2008, Phys Rev E). Classification analyses were performed with a linear support vector machine and a leave-one-subject-pair-out cross validation scheme (k=30). Classification performance measures were evaluated for statistical significance with permutation tests (10,000 iterations).

Results: Whole-brain fractal connectivity matrices provided sufficient pattern-information for above chance classification of diagnostic status (Accuracy=81.67%, Sensitivity=80%; Specificity=83.33%; PPV=82.76; NPV=80.65%; all $p < 9.99 \times 10^{-5}$). This performance stands in stark contrast to conventional measures of functional connectivity measured by Pearson correlation matrices across each wavelet scale (all Accuracy < 73%).

Conclusions: This work demonstrates enhanced sensitivity for 'fractal' connectivity measures for characterizing atypical connectivity in autism compared to conventional correlation measures that are currently in wide use (Pearson's correlation). 'Fractal' connectivity measures diverge from conventional measures of functional connectivity by taking into account the long memory fractal properties of BOLD time-series data. One unresolved question for future work lies in understanding the contributions of neural and non-neural sources influencing fractal behavior in BOLD time-series data. Finally, this work observes levels of classification performance that are statistically significant for deeming important for hypothesis testing, but are not high enough to be useful in a clinical setting or in settings where the base rates of ASC approach the population prevalence. Increases in sample size as well as use of other methods for whole-brain parcellation will also be important for future work.

108.146 146 Functional Brain Maturation in Children and Adults with ASD Across 3 Cognitive Tasks (Attention, Temporal Discounting and Decision-making): An fMRI Investigation. C. M. Murphy*¹, A. Christakou², E. Daly³, C. Ecker³, P. Johnston², A. B. Smith², V. Giampietro², M. Brammer², D. Robertson², D. Spain², M. AIMS², D. G. Murphy⁴ and K. Rubia², (1)King's College London, Institute of Psychiatry, (2)King's College London, Institute of Psychiatry, (3)King's College London, Institute of Psychiatry, (4)Institute of Psychiatry. King's College London

Background:

The cognitive behavioural profile of individuals with autistic spectrum disorder (ASD) includes difficulties with sustained attention, temporal foresight, forward planning and decision-making. However, little is known of the neurofunctional substrates underlying these deficits, nor how functional brain maturation during these crucial cognitive functions may differ in people with ASD.

Objectives:

We used fMRI across 90 children and adults (11-35 years old) with ASD and typically developing controls to investigate 1) differences in brain activation in children and adults with ASD relative to controls during three tasks that measure sustained attention, temporal discounting and decision-making and 2) differences in

neurofunctional maturation in people with ASD relative to controls.

Methods:

46 males (11-35 years old) with ASD and 44 age/IQ matched typically developing male controls completed three event-related fMRI tasks on a 3T MRI scanner. All participants were right-handed, medication-naïve, IQ >70. All individuals with ASD were diagnosed with autism or Asperger (ICD-10) and met ADI and ADOS cut-offs for autism. The 12 minute parametric sustained attention task (SAT) requires subjects to respond as quickly as possible to a timer that appears under two delay conditions: 1) short, frequent, predictable delays (500ms), 2) randomly interspersed long, unpredictable delays (2s, 5s, 8s). Long unpredictable delays place a higher load on sustained attention (parametrically modulated with increasing delays); short predictable delays place a higher load on sensorimotor timing. The 12 minute temporal discounting task (TD) measures the effect of delay on reward-related decision making and temporal foresight. Subjects choose between small immediate rewards and larger delayed rewards. The 20 minute Gambling Task (GT) measures temporal bridging during long-term decision making, reward anticipation and the effects of monetary gain/loss on brain activation. Subjects choose between cards that result in high immediate gain, but larger future loss ("risky": long-term loss), or lower immediate gain, with a large final reward ("safe": long-term gain). Data were analysed using non-parametric image analysis (XBAM: www.brainmap.co.uk). To investigate whether group differences in brain activation were associated with differential neurofunctional development, we performed conjunction analyses between group differences in activation and group differences in whole-brain age correlations.

Results:

SAT: Individuals with ASD had slower reaction times and greater intrasubject variability than controls and underactivated dorsolateral and inferior prefrontal, striato-thalamic, temporal and cerebellar regions. The conjunction analysis showed that most of these regions that differed significantly between groups also differed in functional maturation; they increased

progressively with age in controls, but not in ASD. Furthermore, abnormal activation and functional maturation in frontal regions was associated with poorer task performance and clinical measures of ASD and attention.

TD and GT: data will be presented at the conference.

Conclusions:

Findings suggest that individuals with ASD have significant differences from controls in the functional activation of brain networks central to sustained attention, temporal discounting and decision-making. Importantly, this study shows that functional activation deficits across 3 tasks in ASD are associated with underlying abnormalities in functional brain maturation, suggesting that abnormal brain function may be due to abnormal functional maturation.

108.147 147 Atypical Brain Correlates of Automatic Visual Change Detection in Autism. H. Clery*¹, F. Andersson¹, F. Bonnet-Brilhault², B. Wicker³ and M. Gomot¹, (1)*INSERM U930, Université François Rabelais*, (2)*UMR Inserm U930*, (3)*Institut de Neurosciences de la Timone*

Background: Clinical observations of people with autism spectrum disorders (ASD) show that they react in an unusual way to unexpected changes that appear in their environment. Several studies have examined the neural basis of the automatic novelty detection in patients with ASD in the auditory modality and have highlighted atypical change processing.

Objectives: The aim of the present study was to determine whether these abnormalities in change detection could also be evidenced in the visual modality. This fMRI study was thus designed to localize the brain activations elicited by visual unattended changing stimuli in adults with ASD compared to controls.

Methods: Seventeen healthy adults and twelve patients with ASD participated in the experiment. A passive oddball paradigm in which stimuli consisted in the deformation of a circle into an ellipse either in the horizontal (standard) or in the vertical direction (deviant, $p=0.15$) or into another shape (novel, $p=0.15$) was used. In order

to present the visual stimuli outside the focus of attention, a concurrent task was required in which subjects had to stare at the fixation cross and to respond to its disappearance.

Results: Combined results from all volunteers highlight the involvement of both occipital (BA 18/19) and frontal (BA 6/8) regions in visual change detection. However adults with ASD display stronger activity in the bilateral occipital cortex (BA 18/19) and in the anterior cingulate cortex ACC (BA 32) associated with smaller activation in frontal regions (BA6/8) than controls. To further investigate ACC involvement during automatic change detection, a psychophysiological interaction analysis was performed with ACC as seed. Results show that the ACC is more functionally connected to sensory regions in ASD than in controls, but less connected to prefrontal and orbito-frontal cortices.

Conclusions: To conclude the present work evidenced atypical brain correlates of automatic visual change detection in adults with ASD. Indeed, compared to controls, larger sensory activation associated with reduced frontal activation were highlight in ASD. Besides, atypical psychophysiological interactions between frontal and occipital regions were evidenced, congruent with the idea of atypical connectivity between these regions described in the literature. Moreover, the atypical involvement of the anterior cingulate cortex in visual change detection can be related to previous results obtained in the auditory modality, thus suggesting that abnormalities in change detection are independent of the sensory modality. This supports the hypothesis of an altered general mechanism of change detection in patients with ASD that would underlie their unusual reaction to change.

108.148 148 Functional Magnetic Resonance Imaging in Intellectual Impairment and Autism Spectrum Disorder. A. G. McKechnie*, T. W. J. Moorhead, C. Thorburn, N. Roberts, E. C. Johnstone, D. G. C. Owens and A. C. Stanfield, *University of Edinburgh*

Background:

A major objective of research into autism spectrum disorders (ASD) has been to delineate the affected neural systems, paving the way for the rational development of new therapies. Functional magnetic resonance imaging (fMRI) of

the brain has played a key role in this research, but its application has been limited to affected individuals with preserved or even superior intellectual functioning. This is despite research consistently indicating that many individuals with autism also have co-morbid intellectual impairment. Such individuals are generally excluded from fMRI studies for practical reasons related to difficulties obtaining informed consent, tolerability of the scanner environment and the lack of suitable fMRI tasks which can be completed by intellectually less able individuals. While this is understandable it leads to an unacceptable situation where the existing fMRI research concerns individuals who are not necessarily representative of the broader autism population.

Objectives:

The objective of this study was to demonstrate that it is feasible to reliably use a functional MRI task in individuals with intellectual impairment ± co-morbid autism spectrum disorder (ASD) in a task of implicit emotion processing.

Methods:

We conducted a functional magnetic resonance imaging study using an implicit emotion processing task to examine participants' differential response to images of emotion-laden human faces compared to neutral-expression faces (N=10; ASD=5; age: 25 ± 2.5 years). Diagnosis of ASD was confirmed using the Autism Diagnostic Observation Schedule (ADOS). Prior to undergoing the scan, participants were able to practice the task on a laptop and also to practice on a mock scanner (where there were no time pressures). The block-design fMRI task consisted of 6 blocks of 6 faces of an emotional (Ekman fear faces) or neutral (Ekman neutral faces) type. Each face was shown for 5000ms. Prior to, and between, each block participants were asked to observe a fixation cross. To ensure the participants were attending to the stimuli presented, they were asked to depress a trigger each time they viewed a face. The images were acquired on a Siemens 3T scanner and analysed using SPM5.

Results:

All 10 participants were reliably able to perform the task both in rehearsal and in the real scanner environment. Analysis of the data using voxel based morphometry showed that individuals with ASD had less grey matter in the posterior cingulate (Brodmann area 31). Analysis of the fMRI data revealed reduced signal in the ASD group in areas previously described as associated with emotion processing, confirming findings from studies with non-intellectually impaired individuals.

Conclusions:

In this study we have demonstrated that it is possible to undertake functional magnetic resonance studies in individuals with intellectual impairment, who were previously considered unable to participate in such studies. We have also replicated findings of grey matter tissue loss in individuals with intellectual impairment and comorbid ASD compared to intellectually impaired controls; and decreased cerebral function in brain regions previously linked with emotional processing deficits in non-intellectually impaired individuals with ASD.

108.149 149 Serotonin and Restricted, Repetitive and Stereotyped Behaviors in Autism. E. Daly*¹, C. Ecker¹, C. M. Murphy¹, N. Gillan¹, M. Gudbrandsen¹, V. D'Almeida², D. Robertson¹ and D. G. Murphy³,
(1)King's College London, Institute of Psychiatry,
(2)Centre For Neuroimaging Sciences, Institute of Psychiatry, King's College London, (3)Department of Forensic and Neurodevelopmental Sciences, Institute of Psychiatry, King's College London

Background: People with autism have life-long difficulties in social interaction communication and repetitive behaviours. It has been suggested that the restricted, repetitive and stereotyped behaviors, typically found in autism, are underpinned by deficits of inhibitory control. The biological basis of this is unknown but may include differences in the modulatory role of neurotransmitters, such as serotonin, which are implicated in the condition.

Objectives: In order to assess the modifying role of serotonin on inhibitory brain function in adults with autism and controls we employed acute tryptophan depletion (ATD) and functional Magnetic Resonance Imaging (fMRI).

Methods: We performed a double-blind, placebo-controlled, crossover trial of ATD using fMRI to measure brain activity during a Go/No-Go inhibition task in 14 adults with autism and normal IQ and 14 controls who did not differ in gender, age and IQ.

Results: During SHAM, adults with autism relative to controls had reduced activation in key inhibitory regions of inferior frontal cortex and thalamus, but increased activation of caudate and cerebellum. However, brain activation was modulated in opposite ways by ATD in each group. Within autistic individuals ATD upregulated fronto-thalamic activations and downregulated striato-cerebellar activations toward control SHAM levels, completely 'normalizing' the fronto-cerebellar dysfunctions. The opposite pattern occurred in controls. Moreover, within people with autism, there was a significant relationship between severity of restricted, repetitive and stereotyped behaviors and functional abnormality at baseline within frontal and thalamic regions; and between the degree that this abnormality was reversible by serotonergic modulation.

Conclusions: Individuals with autism have abnormal inhibitory networks, and that serotonin has a differential, opposite, effect on them in adults with and without autism, together these factors may partially explain the severity of restricted, repetitive and stereotyped behaviors in autism and/or provide a novel (tractable) treatment target.

108.150 150 Neural Correlates of Emotion Recognition in Music in Adults with Autism Spectrum Disorder. L. Gebauer*¹, J. Skewes¹, P. Heaton² and P. Vuust¹,
(1)Center of Functionally Integrative Neuroscience, Aarhus University, (2)Goldsmiths College, University of London

Background: Music is a potent source for eliciting emotions, but not everybody experience emotions in the same way. Social and emotional difficulties are core characteristics of autism spectrum disorders (ASD). Difficulties in recognizing emotions from faces and speech are widely studied in ASD, and impairments are associated with differential brain responses. However, whether these difficulties and differential brain responses generalize to music is less clear.

Objectives: The first objective of this study was to investigate the neural correlates of emotion recognition in music in high-functioning adults with ASD. Secondly, we investigated how potential differences in neural activation are related to autistic traits.

Methods: 19 adults with ASD and 21 typically developing adults were scanned using fMRI, while listening to happy, sad and neutral musical excerpts. All participants filled out the Autism Quotient questionnaire (AQ¹), giving a total score and five sub-scores; social skills, attention switching, attention to detail, imagination and communication.

Results: The ASD-group rated happy music as slightly less happy than did the TD-group, and showed increased brain activity in response to happy music in posterior cingulate (PCC), medial prefrontal cortex (mPFC), postcentral gyrus, inferior temporal gyrus and cerebellum. The increased brain activation in these areas was positively correlated with total AQ-score and especially with impaired social skills.

Conclusions: The increased brain activity found in the ASD group in PCC and mPFC is probably associated with memory functions, suggesting that these areas support a compensatory mechanism for recognizing emotions in music in people with ASD. The remaining areas are previously found to be related to increased motor activity and physiological arousal. Thus, we hypothesize that the ASD group show increased physiological arousal in response to happy music, but rely on learned strategies based on previously heard melodies to a greater extent than do typically developed controls. The increased brain activity found in ASDs correlated with impaired social skills, suggesting that social skills are critical for intact emotion recognition and processing of music.

References: Baron-Cohen, S., Hoekstra, R. A., Knickmeyer, R., & Wheelwright, S. (2006). The Autism-Spectrum Quotient (AQ)--adolescent version. *J Autism Dev Disord*, 36(3), 343-350. doi: 10.1007/s10803-006-0073-6

108.151 151 An Investigation of the Role of the Brain GABA-Benzodiazepine Receptor Alpha-5 Subtype in Autism Spectrum Disorder Using the Benzodiazepine Inverse

Agonist PET Ligand [¹¹C]Ro15-4513. M. A. Mendez^{*1}, J. Horder¹, J. F. Myers², S. Coghlan¹, P. R. Stokes³, D. Erritzoe³, O. Howes⁴, A. Lingford-Hughes³, D. J. Nutt³ and D. G. Murphy¹, (1)*Institute of Psychiatry, King's College London*, (2)*Bristol University*, (3)*Imperial College London*, (4)*MRC Clinical Sciences Centre*

Background:

The biological associates of clinical symptoms in Autism Spectrum Disorders (ASD) are poorly understood. An imbalance between gamma-aminobutyric acid (GABA) and glutamate neurotransmission has been suggested to be responsible for the impaired information processing and social behavior described in autism. However, relatively few studies have directly examined brain GABA or glutamate in people with ASD. Recent neurochemical research has focused on the GABA system in a number of limbic regions and its possible causal relationship with symptoms in people with ASD. Nobody has yet directly examined the in vivo availability of brain GABA A receptors in adults with ASD, or related variation in GABA A receptors to symptoms.

Objectives:

To measure $\alpha 1$ and $\alpha 5$ GABA-A subtype receptor levels in limbic regions frequently implicated in ASD: the amygdala-hippocampal complex, basal ganglia and anterior cingulate cortex, using Positron Emission Tomography (PET) with the benzodiazepine receptor PET ligand [¹¹C]Ro-15-4513.

Methods:

Three volunteers diagnosed with Asperger's Syndrome matching the ICD-10 criteria who scored above threshold for ASD in the Autism Diagnostic Observation Schedule (ADOS) and three age-sex matched controls underwent 90 minute, fully quantified [¹¹C]Ro15-4513 PET scans. Structural MRIs were used to localize radioligand binding to specific brain regions. Spectral analysis was used to quantify volume of distribution (V_T) in individual regions of interest, and the contribution of ligand binding at the $\alpha 1$ - and $\alpha 5$ - containing GABA-A receptor subtypes.

Results:

A two-way ANOVA showed significantly lower V_T across all regions in the brains of participants with ASD comparing to controls ($F=140.7$, $p<0.0001$). This effect was largely related to the $\alpha 5$ -containing subtype ($F=32.27$, $p<0.0001$). Further Student t-tests showed significant lower binding in nucleus accumbens ($t=3.360$, $p<0.05$) and amygdala ($t=3.684$, $p<0.05$), and a similar trend in hippocampus and the anterior cingulate gyrus.

Conclusions:

The abnormalities within the limbic system found in this study may explain some of the social and emotional difficulties observed in people with ASD, specifically Asperger's Syndrome, as GABAergic neurons are fundamental for the processing of information in most brain regions.

Though lower levels of $\alpha 5$ appear predominantly responsible for the lower V_T , the low signal:noise ratio of these methods of estimating V_T at the lower affinity $\alpha 1$ -containing subtype, with low subject numbers, limits the certainty of this interpretation. However, the lack of changes in receptor kinetics at either subtype suggests the differences in binding are probably due to down-regulation of receptor expression, supporting previous findings in gene assays.

The understanding of the GABAergic system in more detail through the characterisation of the $\alpha 5$ -containing subtype will allow *in vivo* assessment of the imbalance between the GABA/glutamatergic system that has been postulated in autism and may give us some future guidance in the pharmacological management of ASD.

108.152 152 Large-Scale Cortical Functional Connectivity During Social Scene Processing in ASD. B. Wicker*, *Institut de Neurosciences de la Timone*

Background: From appropriate perception and understanding of another individual's non verbal body behaviour, and its association to various element of the environmental context, humans are able to gain crucial knowledge about the environment and use it to subsequently adapt their own behaviour successfully. This results in a continuous need to rapidly and accurately monitor

social contexts and meanings. Two cognitive systems might have a complementary role in understanding social scenes. Motor and emotional perception and simulation mechanisms may provoke a pre-reflective or automatic representation of the visual scene, whereas inferential mechanisms may then elaborate on this initial hypothesis by using previously acquired conceptual knowledge. An altered capacity to interpret socio-emotional context and use it to adapt their behavior accordingly is a hallmark characteristic of individuals with ASD's behavior.

Objectives: We used functional magnetic resonance imaging (fMRI) to assess the functional connectivity of brain networks involved in the explicit processing of emotional information presented in realistic movie clips depicting everyday social interactions. Because of its role in explicit emotional attribution, we hypothesized that the Dorsomedial Prefrontal cortex (DMPFC) would be abnormally activated and functionally connected in participants with ASD compared to controls.

Methods: Twelve right-handed male adult volunteers (mean age = 21 ± 2 years) and twelve right-handed adults with high functioning autism (HFA) or Asperger Syndrome (AS) (autistic spectrum disorders (ASD); mean age = 26 ± 10) participated in the study. Structural and functional images were acquired on a 3 Tesla Bruker scanner. Stimuli consisted of a set of sixty four 9 sec. video clips of everyday socio-emotional events. We contrasted experimental conditions where subjects were required to process emotional information explicitly or implicitly. To explore large scale connectivity within brain networks, we performed functional connectivity modelling using an atlas of 152 regions of interest derived from a morphometric parcellation of the brain of each individual subject.

Results: Performance levels were identical for both groups, suggesting that adults with ASD are perfectly able to recognize other's emotional behavior when asked to do so explicitly. However, this intact performance in explicit attribution of emotion was associated with an absence of activation of the DMPFC in the ASD group. Furthermore, large-scale functional connectivity analysis revealed abnormal long-range connectivity in the antero-posterior axis, more

specifically between the DMPF_c, lateral prefrontal cortex and precuneus.

Conclusions: Our results using whole social scenes confirm those obtained in previous studies using emotional faces or body movements. A network of brain regions including the DMPF_c seem to be consistently abnormally activated and functionally connected in ASD, suggesting a absence of top-down influence that lead to a difficulty to attribute emotional valence to the otherwise normally perceived stimuli. We discuss these results by underlying the striking similarity between this brain network and both the 'resting state' and the 'contextual' network. Abnormal emotional processing in ASD may be related to abnormal introspection and an altered capacity to associate the stimulus to its affective meaning by reactivating previously acquired conceptual emotional knowledge.

108.153 153 Intact Mirror Neuron Systems in Autism: A Meta-Analysis. A. Hamilton*, *University of Nottingham*

Background:

It has often been claimed that dysfunction of the human mirror neuron system is a key cause of difficulties in imitation and social interaction in individuals with autism spectrum condition. However, this claim is very controversial. A variety of neuroscientific methods have been used to study the integrity of the mirror system in autism, but an overview of these results does not yet exist.

Objectives:

This study aims to evaluate the broken mirror hypothesis of autism, by conducting a systematic review of all neuroscientific studies of mirror neuron function in children and adults with autism spectrum disorder.

Methods:

25 studies were identified which use neurophysiological methods (EEG / MEG / TMS / fMRI / EMG / eyetracking) to examine mirror neuron systems in autism. These were evaluated in terms of whether or not they provide statistically robust evidence for abnormal mirror

neuron responses in autism which cannot be attributed to other effects.

Results:

Considering studies of the MNS which use weakly localised methods (EEG / MEG / TMS / EMG), only the TMS studies (n=2) consistently report differences in autism. EEG (n=8), MEG (n=3) and EMG (n=2) all report mixed results with little clear evidence for abnormal mirror systems. 4 eyetracking studies all report normal behaviour in autism. 8 fMRI studies have directly measured MNS engagement. Studies using emotional stimuli (n=4) report some group differences, while those using non-emotional stimuli (n=4) mostly do not. Structural MRI studies do not report consistent abnormalities of the MNS.

Conclusions:

These data demonstrate that over 10 years after it was first suggested, there is little evidence to support idea that mirror systems are broken in autism or that this failure is a primary cause of poor social skills. I suggest that it is more useful to consider how social cues exert top-down control over imitation responses in ASC (Wang & Hamilton, 2012). In this model, basic visuomotor processing in the mirror neuron system is intact in ASC, but top-down modulation of this system by social signals is abnormal. This top-down model can account for current data and also for new results showing differential imitation of goal-directed and social actions in children with ASC (Marsh & Hamilton, IMFAR poster). Implications of this model for both research and therapies will be considered.

108.154 154 The Influence of Cognitive Load On Working Memory in Children with Autism. V. Vogan*¹, W. Lee¹, B. Morgan¹, M. L. Smith², E. Anagnostou³ and M. J. Taylor¹, (1)*Hospital for Sick Children*, (2)*Research Institute, Hospital for Sick Children*, (3)*University of Toronto*

Background: Children with Autism Spectrum Disorder (ASD) exhibit various cognitive and executive deficits, including working memory (WM), which rely largely on the frontal lobes of the brain. Abnormal maturation of the frontal lobes has been documented in ASD, yet little is known about the link between frontal lobe

function and memory impairments in ASD. We are not aware of any neuroimaging studies of WM in autism; however, recent studies of adults with and without ASD suggest differences in neural activation of WM networks (Luna et al., 2002; Koshino et al., 2008). Studying the development of WM is extremely important as it may provide insight into the underlying cause of autistic symptomatology, and predict functional and academic outcomes.

Objectives: To examine the effects of difficulty level on WM capacity and identify how the neural systems underlying WM differ in children with and without ASD using functional neuroimaging.

Methods: Measures of brain activity were acquired using functional magnetic resonance imaging (fMRI) in 24 children with high functioning ASD (7-13 years; IQ scores of 70 or above) and 24 age matched controls using a visuospatial working memory capacity task. Diagnosis of ASD was confirmed by the Autism Diagnostic Observation Schedule-Generic and Autism Diagnostic Interview-Revised (Lord et al., 2004). The WM task measures the number of items that can be held in mind across six levels of difficulty. Neural activation was assessed between groups as a function of cognitive load (task difficulty level).

Results: Preliminary results show activation in regions associated with WM (dorsolateral prefrontal cortex) in both ASD and control groups. The autism group exhibited more activity than the control group in the frontal regions of the brain, such as the superior frontal gyrus and medial frontal gyrus, across levels of difficulty. Children with autism showed more activation than controls in the anterior cingulate cortex (ACC); however the ASD group did not show change in activity as difficulty varied, whereas controls modulated ACC activity with difficulty. Group differences were also apparent in the precuneus activation.

Conclusions: Patterns of neural activity in children with and without ASD suggest differences in working memory systems between the two groups. Brain activity varied with difficulty level in both groups; however, cognitive demand may only influence selective brain areas in children with ASD. Findings will increase our knowledge of

the neural and cognitive abnormalities of autism, and their links to ASD-related symptoms. These data will allow us to identify the nature of atypical development, which is critical in establishing age-appropriate interventions that can effectively target working memory functions.

108.155 155 Investigating Functional Connectivity in a Large Sample of Children with Autism Spectrum Disorders. B. Deen*¹, R. Saxe² and K. A. Pelphrey³, (1)*Massachusetts Institute of Technology*, (2)*MIT*, (3)*Yale University*

Background: A number of recent studies have investigated functional connectivity in individuals with Autism Spectrum Disorders (ASD), by assessing correlations between fMRI signals from different brain regions. However, results of these studies have been relatively inconsistent, with reports of both underconnectivity and overconnectivity in ASD, in a range of different functional networks. It is not yet clear whether these differences resulted from differences in the specific group of ASD participants recruited in each study, differences in preprocessing or analysis methods used, or differences in the regions and networks investigated. Additionally, many prior studies are subject to potential confounds, including differences in motion across groups, differences in the extent of task-evoked activity, and differences in the effect of global signal removal.

Objectives: To investigate resting-state functional connectivity in a large sample (N=584) of children with and without ASD, using data from the Autism Brain Imaging Data Exchange (ABIDE). Furthermore, we assessed a number of functional networks, and accounted for the confounds mentioned above.

Methods: A subset of subjects from the ABIDE dataset were chosen based on the following criteria: subjects were under age 18 and had an IQ above 70, and their data had nearly full coverage of the brain and lacked gross image distortions. Several novel preprocessing techniques were implemented to eliminate potential confounds: 1) pairs of frames with >.5mm of translation or >.5° of rotation between them were removed from the analysis; 2) instead of global mean removal, data were denoised using CompCorr, a PCA-based technique removing signals from white matter and cerebrospinal fluid.

After preprocessing, a smaller subset was chosen that matched distributions of several motion measures across groups, excluded subjects with more than 25% of volumes discarded due to motion, and matched groups on age and gender. Seed-based functional connectivity analyses were performed using seeds from the default mode, control, dorsal attention, motor and visual networks. Each group-level model accounted for effects of group as well as age, eye status (open or closed), gender, mean translation, mean rotation, and site of data acquisition.

Results: Across networks, functional connectivity maps were highly similar across groups. Small but significant group differences were observed in the motor and control networks, in both directions. Substantial effects of motion, age, and site of acquisition were observed for all networks.

Conclusions: These results indicate that functional connectivity is highly similar in children with and without ASD, calling into question the use of functional connectivity data as evidence for the underconnectivity hypothesis of ASD. Consistent with prior research, motion was found to have a strong and pervasive effect of functional connectivity estimates, stressing the importance of tightly controlling motion in studies comparing functional connectivity across groups. Interestingly, large and reliable differences in functional connectivity were observed across sites, indicating that certain acquisition parameters may be better optimized for this measure.

108.156 156 Atypical Functional Connectivity in Children with Autism Spectrum Disorder Using Magnetoencephalography (MEG). S. Desai^{*1}, L. B. Hinkley², S. S. Hill³, J. Harris¹, A. D. Antovich¹, S. Nagarajan¹ and E. Marco³, (1)*University of California, San Francisco*, (2)*UCSF Autism & Neurodevelopment Program*, (3)*University of California San Francisco*

Background: Previous functional imaging studies of resting-state brain activity in autism suggest altered connectivity in the “default mode” network as well as regional oscillatory power differences. To date, there are no published reports of resting state whole brain non-phase lagged alpha-band coherence using magnetoencephalography (MEG) to assess children with autism. MEG is a functional imaging technology that quantifies the magnetic activity generated by electrical currents in the brain. We

can estimate the degree to which the neurons in specific brain areas (voxels) are firing synchronously with other voxels in the brain – with millisecond temporal resolution and centimeter spatial accuracy. In our previous work, we report atypical somatosensory cortex activation that is directly correlated with observed tactile sensory behavior. Thus we were motivated to investigate both the differences in whole brain coherence between groups as well as the specific coherence related to tactile processing ability.

Objectives: The aim of this study is to determine if boys with autism show altered resting state connectivity relative to age, gender, and performance IQ matched healthy controls (HC) using MEG functional coherence. We also sought to explore whether behavioral measures of language and social skills and direct sensory assessment of tactile processing is related to the measured neural cortical connectivity.

Methods: Resting activity (eyes closed) was recorded for the autism cohort who met ADI-R and ADOS ASD criteria (n=20, mean age=9.25y) and the HC group (n=25, mean age=9.64y) using 275-channel whole-head MEG (CTF Inc.). Oscillations in the alpha-band (8-12Hz) across a 60 second window were isolated from 4 minutes of continuous recording. Neural sources were estimated using an adaptive spatial filtering technique and functional connectivity was computed using global imaginary coherence. Connectivity volumes were compared between the ASD and HC groups. Voxelwise correlations between global connectivity and autism-related language and social deficits (SCQ) as well as direct measures of somatosensory processing (graphesthesia) were calculated.

Results: The ASD cohort was found to show significantly higher connectivity in three regions: the dorsal medial superior frontal gyrus (D-mSFG), ventral medial superior frontal gyrus (V-mSFG), and precuneus (FDR corrected <5%). Behavioral-Coherence correlations revealed that increased language impairment is directly correlated with higher connectivity of the implicated D-mSFG region for the ASD but not the HC cohort (ASD: $r=0.634$, $p<0.002$; HC: $r=-.138$, $p=0.51$). No correlations were found with the social construct of the SCQ. We found additional correlations between measures of tactile

processing and right precentral gyrus connectivity (Brodmann area 4) for both groups. This suggests that the degree of coherence in this region may predict ability beyond the confines of diagnostic labels even though the ASD group performs significantly worse on graphesthesia accuracy (ASD mean=18.16, HC mean=21.61, $p=0.02$).

Conclusions: School-aged boys with autism show increased resting coherence in medial anterior and posterior regions within the default mode network suggesting an over engagement in regions serving internal preoccupation/reflection and a dysfunction of connections between critical brain regions. Furthermore, we observe a range of connectivity in the primary somatosensory region that may be used to predict tactile processing ability.

108.157 157 Numerosity Estimation in Autism: A MEG Study. E. Meaux^{*1}, M. J. Taylor², E. W. Pang² and M. Batty¹, (1)*INSERM U930*, (2)*Hospital for Sick Children*

Background:

Our ability to manipulate numerical quantities and especially to estimate and compare them is a fundamental skill, by which we make sense of the external world. In addition to the core triad of symptoms that characterize Autism Spectrum Disorders (ASD), exceptional visual skills are frequently reported, including superior abilities in numerosity estimation. This phenomenon has been addressed by two theories which argue that people with ASD perceive the world differently, the weak central coherence hypothesis (WCC) and the enhanced perceptual function hypothesis (EPF). These hypotheses attribute the superior performance on numerosity estimation displayed by individuals with ASD to their specific processing of local features, rather than focusing on the whole Gestalt. However, superior skills for numerosity estimation could also result from superiority in numerosity process itself.

Objectives:

The current study examined the neural substrates of numerosity estimation, in young adults with and without autism, to disentangle perceptual atypicalities from aspects of numerosity processing itself.

Methods:

Fourteen adults with ASD diagnosed according to the DSM IV criteria, without mental retardation, were matched with 14 typically developing (TD) adults. Participants were asked to estimate the number of dots (between 80 and 150) arranged either randomly (local information) or in a meaningful pattern (global information) while brain activity was recorded by magnetoencephalography (MEG). Source analyses were performed within the time windows determined by analysis of the sensor data using an event-related beamformer algorithm, first, for all stimuli and then according to the meaningfulness of the stimuli. Only statistically significant source differences are described.

Results:

Behavioural results showed no enhanced numerosity processing abilities in ASD participants. However, analyses of **MEG** data revealed significant differences in brain activation during this process between ASD and TD subjects. At an early stage of numerosity estimation (80-120ms), significant differences in source amplitude of activation (TD > ASD) were found in the visual areas, in the lingual gyrus and cuneus. From 120 to 400ms, group differences extended to first temporal and then parietal regions, showing greater activation in TD subjects in the precuneus, middle temporal gyrus, superior parietal lobule and inferior parietal lobule. Finally, after 400ms, a source was found in the superior frontal gyrus in TD but not in ASD participants. Moreover, in TD participants, the activation in the temporal areas between 120-290ms was sensitive to the global arrangement of the dots (global>local). This effect was not observed in ASD participants for whom an inverted effect (local>global) appeared later in this brain region (after 290ms).

Conclusions:

Brain responses during numerosity estimation are atypical in autism. We suggest that the early occipital differences could be explained by sensory abnormalities already observed in ASD. Differences in temporal regions could be linked to perceptual atypicalities, specifically, differences in

sensitivity to global perception. Interestingly, our MEG data demonstrated that parietal and frontal activations known to be involved in numerosity processes also are affected in ASD. Taken together, these results suggest that the atypical number estimation ability seen in ASD may be due to “overlapping impairments” in sensory, perceptual and numerosity processing.

108.158 158 Sex-Differential Fractal Complexity of Resting-State Brain Oscillations in Autism. M. C. Lai*¹, M. Lombardo², B. Chakrabarti³, A. N. Ruigrok⁴, E. T. Bullmore⁴, S. Baron-Cohen⁴, M. A. Consortium⁵ and J. Suckling⁴, (1)Autism Research Centre, Department of Psychiatry, University of Cambridge, (2)University of Cambridge, Autism Research Centre, (3)University of Reading, (4)University of Cambridge, (5)University of Cambridge, Institute of Psychiatry, University of Oxford

Background: Fractal properties of resting-state fMRI BOLD signal oscillations have been shown to be atypical in adult males with autism spectrum conditions (ASC). Fractal scaling in males with ASC is shifted more towards randomness (Lai et al., 2010, Biol Psychiatry) suggestive of a ‘noisier’ resting-state signal in ASC. Given the emerging evidence of sex-differential characteristics of ASC, it remains to be seen how biological sex affects the fractal properties of resting-state oscillations as a potential fundamental characteristic of the neurobiology of ASC.

Objectives: To investigate if the fractal properties of resting-state brain oscillations affect ASC differently according to biological sex.

Methods: Four groups of right-handed adults (33 neurotypical males and 29 females, 25 males and 30 females with ASC; aged 18-49 years), matched for age, IQ and in-scanner head motion, were scanned with fMRI at 3T for 13 minutes (TR=1302 ms). Participants were only instructed to keep their eyes closed and stay awake. We measured at each voxel the Hurst exponent (H), which quantifies the fractal complexity of the resting-state fMRI time series, using a maximum likelihood estimator in the wavelet domain. With whole-gray matter (GM) H -maps, we used a linear support vector machine (L2-regularization and loss, ‘leave-one-subject-pair-out’ cross-validation, executed in LIBLINEAR) to classify individuals by their diagnostic status solely based on multi-voxel patterning of H -maps. Classification analyses were done within-sex in order to test predictive power

of diagnostic classifications without the potential confound of sex. If sex is not a confounder we would expect similar levels of classification performance across each within-sex analysis. Classification performance was evaluated against the null hypothesis with a permutation test (1,000 iterations). Univariate analysis was also implemented with a voxel-wise two-way factorial design (factors of diagnosis and sex), with permutation inference at the cluster level (error cluster per image=1), to identify regions with a significant diagnosis-by-sex interaction.

Results: Within males, multi-voxel pattern-information from GM H -maps were significantly above chance in accuracy of diagnosis predictions (76%, $p=.001$), sensitivity (70%, $p=.03$), specificity (82%, $p=.001$), positive predictive value (PPV, 79%, $p=.001$), and negative predictive value (NPV, 73%, $p=.003$). However within females, H -maps failed to provide pattern-information for significant classification performance above chance conditions (accuracy 42%, $p=.89$; sensitivity 37%, $p=.95$; specificity 47%, $p=.57$; PPV 41%, $p=.90$; NPV 42%, $p=.80$). Univariate factorial analysis revealed 3 clusters showing a significant diagnosis-by-sex interaction ($p=.003$), involving bilateral medial temporal lobes, lingual gyri, left insula and temporal pole, cerebellum and midbrain. The interaction was driven by lower H (i.e., shift-towards-randomness) in males with ASC compared to neurotypical males, whereas no difference was found in H between the female groups. In addition, neurotypical females had a significantly lower H than neurotypical males.

Conclusions: Fractal scaling of resting-state fMRI brain oscillations provides sufficient multi-voxel pattern-information for predicting diagnostic status of ASC in adult males but not in females. These findings suggest importance for characterizing neural mechanisms for autism separately for each sex.

108.159 159 The Autism Brain Imaging Data Exchange (ABIDE): Analytical Approaches and Initial Results. A. Di Martino*¹ and A. Autism Brain Imaging Data Exchange (ABIDE) Consortium², (1)NYU Langone Medical Center Child Study Center, (2)Multiple Organizations

Background: The Autism Brain Imaging Data Exchange (ABIDE) consortium is a grassroots

initiative aggregating and openly sharing to the scientific community over 1100 existing resting state fMRI (R-fMRI) data of individuals with Autism Spectrum Disorders (ASD) and age-matched typical controls (TC). This unprecedented neuroimaging dataset allows testing and generating new hypotheses in ASD.

Objectives: To demonstrate the feasibility of ABIDE to promote progress in understanding the neurobiology of ASD through discovery science. As a first step, given the increasing convergence in the ASD field on dysconnections among brain regions rather than local abnormalities, we focused on R-fMRI data which are particularly suitable for examining intrinsic functional connectivity (iFC).

Methods: Following examination and summary of the phenotypic characteristics of the sample (1112 datasets; 539 with ASD and 573 TC; 7-64 years), we carried out 1) full-brain iFC analyses for both structural and functional parcellation schemes (i.e., structural: Harvard-Oxford Atlas (HOA; Kennedy et al., 1998), functional: Craddock et al., 2012 [Crad-200]); 2) regional voxel-wise measures of iFC including regional homogeneity, voxel mirrored homotopic connectivity (VMHC), seed based iFC of the default network (DN), and fractional amplitude of low frequency fluctuations. Group analyses, limited to males, accounted for age, FIQ, site, and mean framewise displacement (FD) correcting for voxel-wise multiple comparisons with Gaussian random field theory ($Z > 2.3$ and cluster-level $p < 0.05$). For whole brain parcellation-wise correlation analyses, corrections for false discovery rates were applied.

Results: Sample demographics reflect the current status of the neuroimaging field. Despite the lack of *a priori* coordination, most sites used standardized phenotyping applying the Autism Diagnostic Observation Schedule and the Autism Diagnostic Interview-Revised. We also identified factors that vary across studies, to guide future efforts to increase standardization. For example, DSM-IV-TR diagnoses were provided by 80% of sites; consistent with previous multi-site findings (Lord et al., 2012), sites varied markedly in DSM-IV-TR subtype distributions. While whole brain analyses revealed both hypo- and hyper-connectivity in ASD, hypo-connectivity dominated.

Consistent with prior work, in ASD we found reduced iFC involving key DN nodes such as posterior cingulate cortex and dorsomedial prefrontal cortex, and reduced VMHC in sensorimotor cortex. Regional analyses highlighted ASD-related abnormalities in the thalamus, caudate, and insula.

Conclusions: The feasibility of establishing the ABIDE dataset reflects the rapid adoption of R-fMRI approaches in neuroimaging of ASD along with the benefits of standardized diagnostic assessment protocols. Evidence from this initial survey of the unprecedented ABIDE R-fMRI data provides demonstrations of both replication and novel discovery. It also demonstrates the vast information latent in any single functional imaging dataset, and the extraordinary statistical power available from combining datasets across investigators, labs, and countries. By pooling multiple international datasets, the ABIDE sample allows for replication, secondary analyses and discovery efforts, and is expected to accelerate the pace of discovery for the next generation of ASD studies.

108.160 160 Is Autism Characterized by Enhanced Variability in Task-Related Brain Activation?. M. P. Poulin-Lord^{*1}, E. B. Barbeau¹, F. Samson¹, I. Soulières² and L. Mottron¹, (1)Centre d'excellence en Troubles envahissants du développement de l'Université de Montréal (CETEDUM), (2)University of Quebec in Montreal

Background: Autism is characterized by a large diversity among symptomatic profiles and an important heterogeneity in individual developmental trajectories. One possible explanation for this variability in the autistic population is increased cerebral plasticity, the mechanism by which neural pathways can be modified by changes in neural processes. A wide range of studies has documented differences in autistics compared to typical controls in cerebral activation and performance, for example, during tasks involving visual and motor stimuli (Samson et al, 2011., Müller et al, 2004., Soulières et al, 2011). Enhanced cerebral plasticity is likely to be involved in these group differences, more specifically at the level of greater individual variability in the autistic group.

Objectives: The aim of the study is to use functional magnetic resonance imaging (fMRI)

to determine whether there is enhanced variability in autism, in localization and intensity of cerebral activation within modalities that have already shown group differences.

Methods: Groups of 23 autistic and 22 typical participants matched on age (14-36 years old), FSIQ, Raven scores, and laterality performed a visuo-motor imitation task in an MRI scanner. Participants were instructed to imitate 96 visually presented hand gestures with the specified hand. SPM8 was used to study task-related brain activation in visual and motor regions of interest (ROI) at the group and individual level. For each participant the coordinates of the maximum activation peak were extracted in primary (Brodmann area 4) and supplementary (Ba6) motor areas, primary (Ba17) and associative (Ba18+19) visual areas as well as in the fusiform gyrus (FG). An average coordinate for each group and for each ROI was computed by averaging all the individual stereotactic coordinates. For each ROI, each participant's distance to his respective group average was then used as a variable of interest to determine group differences in variability. The same procedure was used to extract the beta value to evaluate differences in variability of intensity. A mixed-effects statistical model was then used to compare groups.

Results: Between group analysis showed more activation in autistics in associative visual areas (V4+Ba18) and the supplementary motor area, whereas controls showed more activity in parieto-occipital junction (V5) and extrastriate cortex (Ba19) ($p < .05$, FWE). Individual distances to the group mean were significantly higher in the autistic group than in the control group for the primary motor area ($p = .01$) and associative visual areas ($p = .002$). The opposite was observed for the primary visual area, where the distances were higher in the control than in the autistic group ($p = .002$). No between-group difference was observed for FG and for intensity of activation ($p > .05$).

Conclusions: Our results suggest that variability occurred in autism only in localization of activation, which was not generalized to all regions but was specific to some areas/modalities. The variability among autistics was not observed in some expected regions, e.g., the FG. Variability was not necessarily associated with regions in

which differences in activation at the group level were observed. These results are consistent with an enhanced variability in the functional allocation of certain brain regions in autism.

108.161 161 The Impact of a Visualization Language Intervention On Brain Activation and Connectivity in Children with Autism. D. L. Murdaugh*, M. L. Morris, A. R. Lemelman, 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. Such increased reliance on visuospatial regions may also underlie weaker coordination between primary visual and association areas in ASD, especially while processing complex language tasks. Of especial interest is the atypical brain activation and weaker connectivity in autism and how such connections can be strengthened through cognitive and behavioral intervention.

Objectives: This fMRI study investigates brain activation and connectivity patterns, using a visual imagery language task, in a longitudinal design before and after a 10-week visualizing language intervention in high-functioning children with ASD. The main objective is to determine whether deficits in functional activation and connectivity are reversible and how such changes reflect behavior.

Methods: Currently, 14 children with ASD (ages 8-13 years) have taken part in a pre-imaging session, with 8 children receiving the intervention soon after the initial fMRI scan, and 6 wait-list control children. Seven children so far have returned for the post-imaging session, 3 having received the intervention between scans, and 4 wait-list controls. A language comprehension task, presented while the children underwent fMRI, included high and low imagery sentences. This 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) In children with ASD ($n = 14$), the pre-intervention brain response to visual imagery sentences included frontal regions (e.g., left

middle frontal gyrus, superior frontal gyrus, dorsolateral prefrontal cortex, and Broca's area) and visual regions (e.g., lingual gyrus and middle occipital gyrus); (2) Greater activation was found in posterior brain regions (i.e., left precuneus and posterior cingulate cortex) when interpreting high imagery compared to low imagery sentences; (3) Children with ASD who received the intervention between imaging sessions ($n = 3$) showed a trend towards increased activation in the medial prefrontal cortex pre-to post-imaging session. This trend was not seen in the wait-list controls ($n = 4$); (4) Lower symptom severity on the Social Communication Questionnaire (SCQ) was correlated with greater activation in frontal regions (e.g., left middle frontal gyrus and Broca's area) at the post-intervention imaging session; (5) A functional connectivity analysis revealed a trend of greater synchronization between Broca's area and the rest of the language network in the children with ASD who received the intervention ($n = 3$) compared to the wait-list controls ($n = 4$).

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. Our preliminary findings reveal the plasticity of the brain in children with ASD, and suggest improvement of neural activity and synchronization due to targeted intervention. We highly anticipate further interesting results as we continue to recruit participants for this study.

108.162 162 An Activation Likelihood Estimation Meta-Analysis of Social Cognition in Autism Spectrum Disorders. M. Patriquin¹, L. Libero² and R. K. Kana², (1)*Virginia Tech*, (2)*University of Alabama at Birmingham*

Background:

Recent perspectives on psychiatric diagnosis encourage researchers to seek objective and quantifiable markers of dysfunction (Montague et al., 2012). In autism spectrum disorders (ASD), broadly consistent findings have pointed to multiple brain regions, e.g., superior temporal sulcus (Kaiser et al., 2010) and fusiform face area (Spencer et al., 2011), associated with deficits in social cognition. These findings underscore the

role of social brain structures by themselves and/or their functional connectivity (Kana, Libero, Moore, 2011) in the neuropathology of ASD. The present study set out to isolate the most critical components of social brain abnormality in individuals with ASD to gain further insight into their social deficits.

Objectives:

The goal of this study was to identify common and consistent spatial locations in the brain, as spatial probability distributions, that underlie social cognition in ASD.

Methods:

This metaanalysis involved a systematic review of all functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) studies that utilized social cognition tasks (e.g., theory-of-mind, face processing, empathy, biological motion, self-other representation) in children and adults with and without ASD. Following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement guidelines, 37 studies were identified that used fMRI and PET techniques. Inclusion criteria were: 1) studies that contained a control and an ASD group of participants; 2) studies with control > autism comparison coordinates for activation reported; 3) studies that used PET or fMRI methods; and 4) studies that were published in English. Activation foci from studies meeting inclusion criteria ($n = 37$) were subjected to a quantitative voxel-based meta-analysis using activation likelihood estimation (ALE; Laird et al., 2005; Laird, Lancaster, & Fox, 2008; Turkeltaub et al., 2002) in GingerALE. ALE maps are then obtained by computing the union of activation probabilities for each voxel.

Results:

Between-group comparisons showed that ASD participants had significantly reduced probability of activation, compared to controls, in areas consistently activated to social tasks: amygdala, superior temporal gyrus (STG), inferior frontal gyrus (IFG), insula, middle temporal gyrus (MTG), fusiform gyrus (FFA), anterior cingulate cortex (ACC), and angular gyrus (AG) ($p < 0.05$,

corrected for multiple comparisons using FDR). Some areas not commonly or primarily associated with social cognition tasks also demonstrated significantly higher likelihood of activation in controls relative to ASD: putamen, parahippocampal gyrus, cerebellum, and thalamus.

Conclusions:

Results indicate significantly reduced engagement of key social brain areas in children and adults with ASD, including amygdala, STG, IFG, and FFA. Medial prefrontal cortex and orbitofrontal cortex, two additional areas considered to be part of the social brain network, were not found to be significantly reduced in ASD participants. The findings from this study synthesize results from existing neuroimaging data on social cognition in ASD, helping to elucidate the network of social brain regions perhaps responsible for the social impairment that is hallmark to ASD.

108.163 163 Neurodevelopmental Trajectory of Emotional Attribution in Autism. L. E. Libero*, C. E. Stevens and R. K. Kana, *University of Alabama at Birmingham*

Background: The ability to interpret others' body language is a vital skill that helps us infer their thoughts and emotions. However, individuals with autism have been found to have difficulty in understanding the meaning of people's body language, perhaps leading to an overarching deficit in processing emotions (Moore et al., 1997; Hubert et al., 2007; Atkinson, 2009; Philip et al., 2010). There are only a few studies examining the neural bases of bodily emotions in autism (Grezes et al., 2009; Hadjikhani et al., 2009). The present study investigated the developmental trajectory of body-centered action and emotion in children and adults with autism.

Objectives: To investigate the neurodevelopmental changes underlying emotion and action, in the context of processing body language, in high-functioning children and adults with autism.

Methods: fMRI data was acquired from 17 children and 15 adults with high-functioning autism, and 16 children and 16 adults as typically developing controls, while they made emotion and action judgments about a series of static stick

figure characters. The participants' task was to view a character's posture and choose the option, from three alternatives, that best described the action (e.g., pushing) or emotion (e.g., sad) the character was portraying. The stimuli were presented in a blocked design format and the data were acquired on a Siemens 3T scanner and analyzed using SPM8 and Group ICA Toolbox.

Results: The main results are as follows: (1) Overall, processing body language activated bilateral inferior parietal lobule (IPL) and bilateral inferior frontal gyrus (IFG) ($p=0.001$, $k=50$). Activation in these areas became more robust moving from children to adults; (2) A simple regression using age as a covariate revealed a positive relationship between age and activation of left IFG, left postcentral, and left superior frontal cortex for judging emotional postures in participants with autism; (3) Comparing children with ASD to their TD peers, there was reduced activation in children with ASD in bilateral middle and inferior frontal cortex ($p=0.005$, $k=20$) while processing emotions; (4) An Independent Component Analysis revealed IPL, IFG, and medial prefrontal cortex (MPFC) as the primary component. Group comparison indicated significantly reduced coherence in RIPL, MPFC, and RIFG for the ASD participants compared to the control participants ($p=0.005$, $k=50$).

Conclusions: The IFG and IPL are two main components of the human mirror neuron system (MNS) associated with the understanding of motor actions (Rizzolatti et al., 1996; Iacoboni et al., 1999). All participants in our study engaged these regions while interpreting body language, indicating the possible use of a mirror mechanism to infer emotions from body postures. Reduced frontal cortex response in children with ASD may suggest a potential difference in the developmental trajectory of their frontal cortex. As participants with ASD increased in age, brain response in IFG and superior frontal areas increased. This may suggest a delay and/or deviance in development of the brain in ASD.

108.164 164 Discriminative Potential of MEG Coherence Imaging of Averted Eye Gaze Processing in Autism Spectrum Disorders. R. Lajiness-O'Neill*¹, A. E. Richard², J. E. Moran³ and S. M. Bowyer³, (1)*University of Michigan Health System*, (2)*Eastern Michigan University*, (3)*Henry Ford Hospital*

Background: While brain activation during tasks requiring eye gaze processing has consistently been found to be abnormal in autism spectrum disorders (ASD), the literature has not provided a coherent understanding of the neural processes underlying abnormal eye gaze processing. The central role of gaze processing impairment in ASD makes this an excellent focus for elucidating aberrant patterns of connectivity.

Objectives: This study investigated (1) whole-brain patterns of coherence during viewing of direct and averted eye gaze in ASD compared to neurotypicals (NT), and (2) the potential diagnostic utility of functional connectivity during gaze processing using discriminant analysis to differentiate groups.

Methods: 11 ASD and 8 NT adolescents and young adults passively viewed images of a character with direct or averted gaze while undergoing magnetoencephalography (MEG). A conditional button press ensured engagement. Synchronicity of the oscillating neurons was measured utilizing a Coherence imaging technique (ICA-MR-FOCUSS). Coherence values were calculated for each pair of 54 brain regions within each of 3 frequency bands: (1-15 Hz), beta (15-30 Hz), and low gamma (30-45 Hz). A between-groups *t*-test was conducted on each pair of brain regions for each frequency band within each condition (direct and averted). The False Discovery Rate method was controlled at 0.1 to correct for multiple comparisons. Of the pathways identified with significant between-group differences, coherence values with a difference > a standard deviation (SD) of 4 and without excessive within-group variance (≥ 0.15 SD) were entered into a linear discriminant analysis using leave-one-out cross-validation.

Results: Averted gaze in the 1-15 Hz band: ASD showed higher coherence between left parieto-occipital regions and right temporo-parieto-occipital regions and lower coherence between bilateral frontal and right fronto-temporo-parietal regions. In the beta band (associated with long range connectivity): ASD showed higher coherence between left parieto-occipital regions and bilateral temporo-occipital and left parietal regions. In the gamma band (associated with short range transmission): ASD showed higher coherence between bilateral temporo-parieto-

occipital regions as well as bilateral parietal and orbitofrontal regions. In both beta and gamma bands: ASD showed lower coherence between bilateral frontal and right superior temporal regions. No significant differences were found during direct gaze. Of the pathways entered into the linear discriminant analysis, six were in the beta band and showed higher coherence in NT than ASD, and one was in the gamma band and showed higher coherence in ASD than NT. Linear discriminant analysis yielded 100% correct classification of both ASD and NT in the beta and gamma bands.

Conclusions: Results provide preliminary support for increased coherence in posterior, short range connectivity and decreased coherence in anterior to posterior, long- and short-range connectivity in ASD while viewing averted gaze. Neural synchrony between frontal cortex and pre- and postcentral gyri, and between frontal and superior temporal cortex in the beta band, and between angular and fusiform gyri in the gamma band were particularly discriminative. The high rate of correct classification of ASD vs. NT using coherence imaging in these pathways during passive viewing of averted gaze suggests it has potential diagnostic utility as a biomarker.

108.165 165 Increased Posterior Cortical Recruitment Mediates Shift From Local to Global Processing in Children with Autism. S. L. Kumar*, H. M. Wadsworth and R. K. Kana, *University of Alabama at Birmingham*

Background: Enhanced performance of individuals with autism on tasks such as the Embedded Figures Test (EFT) and the Block Design Test (BDT) has been attributed to their increased reliance on local details (Plaisted et al, 2003; Mottron et al, 2003). There are only a few neuroimaging studies targeting global and local processing in autism (Damarla et al., 2010; Liu et al., 2011; Ring et al., 1999), with main findings of increased posterior brain activation in participants with autism. While these studies have focused on adults with autism, the main goal of the present study is to probe the neural circuitry underlying the global and local processing in children with autism.

Objectives: The main objective of this fMRI study is to examine the neural bases of global and local processing in children with autism.

Methods: Eleven high-functioning children with autism (age range: 10-15 years) and thirteen age-and-IQ-matched typical control participants took part in this fMRI study. The stimuli, presented in an event-related design, consisted of larger geometric shapes made out of different smaller geometric shapes. Participants were prompted to identify the bigger picture in some trials (global condition) or alternatively to identify the smaller components of the bigger picture in the remaining trials (local condition). The fMRI data collected from a Siemens 3.0T MRI scanner were analyzed using Statistical Parametric Mapping (SPM8).

Results: Analysis of behavioral data revealed intact task performance in participants with autism with no significant group difference in accuracy (Control: Local-83%, Global-86%; Autism: Local-79%, Global-77%) or latency (Control: Local-2606ms, Global-2648ms; Autism: Local-2534ms, Global-2358ms). Within group brain responses suggest robust activation in superior parietal and occipital areas in both autism and control groups during local and global processing. Between group contrasts revealed significantly greater activation in autism in bilateral precuneus, right middle temporal gyrus, and right lingual gyrus during global processing ($p < 0.005$, cluster size = 90 mm³). Further analysis using parameter estimates also showed increased recruitment of the precuneus in autism during global processing.

Conclusions: A more expansive pattern of brain activation in global processing in autism may imply the need for participants with autism to recruit more areas in order to overcome a potential default local-oriented processing. It should be noted that the behavioral performance was intact, but not superior, in participants with autism both in local and in global processing, perhaps attributed to a local advantage manifested only in open tasks (Plaisted, 2001). Increased activation in autism in the lingual gyrus and right middle temporal area is perhaps indicative of more effort in global processing (Fink et al., 1996; Han et al., 2002; Seymour, 2008). In addition, precuneus activation in autism suggests the shift in attention from local (default in autism) to global shape (Himmelbach et al., 2009). Therefore, the shift from local to global processing

in autism may require additional effort at the neural and cognitive levels.

108.166 166 Brain Response to Fearful Faces in ASD with Regression: Research Update. A. Westphal^{*1}, C. Cordeaux², A. Voos³, B. C. Vander Wyk⁴, M. D. Kaiser⁴ and K. A. Pelphrey², (1)*Yale Child Study Center*, (2)*Yale School of Medicine*, (3)*UC Santa Barbara*, (4)*Yale University*

Background: Autism spectrum disorders (ASD) are disorders of early brain development, their ultimate phenomenology thought to be a manifestation of the cumulative results of an atypical developmental trajectory. However, some children undergo regression, developing ASD after a period of typical development, a natural history of illness that is difficult to reconcile with a cumulative explanation. This suggests the possibility of a distinct pathophysiological process. These include children with the diagnoses of Childhood Disintegrative Disorder (CDD) as well as children with other ASDs that appear after a period of normal development. The initial period of typical development of children with regression suggests that the early development of the social brain may follow a typical trajectory, raising the possibility that aspects of its social function will be preserved and evident on functional scanning.

Objectives: To compare subjects with regressive ASD to subjects with non-regressive ASD and typical subjects in terms of brain response to fearful faces.

Methods:

Subjects with regression were defined by positive response to Autism Diagnostic Interview questions 11 and 20, with further detail provided by ADI loss supplement, and a detailed developmental history conducted by a clinician with expertise in regression in ASD. Subjects were only included if they experienced a regression in multiple domains at greater than twenty months of age. Subjects with an ASD, but less dramatic regression were excluded from the analyses. Using a task designed to probe functional characteristics of the social brain, we compared subjects with ASD ($n=34$) to those with regressive ASD ($n=19$) and typical controls ($n=19$) using fMRI (whole-brain scanning, TR = 2s, 3T MRI scanner). Participants with an ASD met diagnostic criteria by the Autism

Diagnostic Observation Scales (ADOS) and ADI scores and clinical evaluation. IQ was measured by overall Differential Ability Scales (DAS) scores, except for several cases of low-functioning children when ratio estimations were made (mental/ chronological age).

Results: Preliminary results of a group comparison between the subjects typical subjects and those with non-regressive ASD are consistent with previous studies, suggesting distinguishing patterns of activation in key nodes of the social brain including the right superior temporal sulcus and bilateral amygdalae in response to fearful faces. Preliminary results of a group contrast between the subjects with regressive ASD and non-regressive ASD indicate significant differences in the right superior temporal sulcus and amygdalae, with the regressive ASD subjects exhibiting patterns of activation more consistent with typical development.

Conclusions: Preliminary data supports the hypothesis that there are functional differences in the activation of several brain areas related to the processing of social information when subjects with regressive ASD are compared to their peers with non-regressive ASD as well as their typically developing peers, supporting the hypothesis that the differences in the onset patterns of ASD may reflect distinct mechanisms.

108.167 167 Disrupted Effective Connectivity Underlying Self-Other Representation in Autism. C. E. Stevens^{*1}, H. D. Deshpande¹, C. L. Klein², M. R. Klinger³, L. G. Klinger⁴ and R. K. Kana¹, (1)*University of Alabama at Birmingham*, (2)*Marietta College*, (3)*University of North Carolina - Chapel Hill*, (4)*University of North Carolina*

Background:

Disruption in interregional functional and anatomical connectivity has been at the center stage of the neurobiological accounts of autism spectrum disorder (ASD) (Just et al., 2012; Kana, Libero, & Moore, 2011). While the insights gained from these models are valuable, functional connectivity does not provide insight into the time-lagged causality and directionality of connectivity. Effective connectivity, on the other hand, provides information about the influence one system exerts over another with respect to a given experimental context (Büchel and Friston,

2000) and tests the direction of connectivity effects. Only a handful of studies have utilized effective connectivity in ASD (Shen et al., 2012; Shih et al., 2010; Wicker et al., 2008). The present study examined effective connectivity in ASD during a self-other judgment task.

Objectives: The main objective of this fMRI study was to examine social information processing in ASD with specific focus on effective connectivity among different brain areas.

Methods:

18 high-functioning adolescents and adults with ASD and 18 age-and-IQ-matched typically developing control participants took part in this study. Participants made "yes" or "no" judgments of whether an adjective, presented visually, described them (*self*) or their favorite teacher (*other*). The data were collected using a 3T MRI scanner. Mean time series was extracted from 5 different regions of interest (ROIs) for all participants. These were the LIFG, LIPL, LMPFC, SMA, and the Caudate nucleus. The extracted time series were normalized and the hemodynamic response de-convolved using a cubature Kalman filter (Havlicek et al., 2011) to get the underlying neuronal response, which were input into the multivariate autoregressive model (Deshpande et al., 2010) and connectivity matrices were obtained for all participants. After this, a *t*-test was performed on the connectivities to examine the paths which were significantly different between the groups ($p < 0.05$ corrected).

Results:

We found an overall significant reduction in effective connectivity across the task in ASD participants relative to control participants. Group differences in connectivity were found primarily in the *other* condition, where the participants with ASD showed weaker effective connectivity from SMA to Caudate [$t(34)=2.03$, $p < 0.05$], MPFC to LIFG [$t(34)=2.04$, $p < 0.05$], LIPL to LIFG [$t(34)=2.03$, $p < 0.05$], and between SMA and LIFG [$t(34)=2.03$, $p < 0.05$], [$t(34)=2.04$, $p < 0.05$] bi-directionally. The only pathway in which effective connectivity was significantly greater for the ASD group was MPFC to Caudate [$t(34)=2.03$,

$p < 0.05$]. In whole-task comparisons, no pathway showed greater effective connectivity in ASD.

Conclusions:

Group differences in effective connectivity emerged only for the *other* condition, with significantly weaker connectivity in ASD in many regions. It should be noted that the connections that were weaker in ASD involved regions that are associated with self-other representation and social cognition. The MPFC has been associated with theory-of-mind and thoughts about others (Ebner et al., 2011), the IFG, IPL, and caudate have been found to have a role in self-other processing (Decety and Somerville, 2003; Kelley et al., 2002). Overall, the findings of this study underscore altered patterns of information flow in participants with ASD during social cognition and supplement functional connectivity findings in ASD.

108.168 168 Neural Correlates of Implicit Contextual Learning in Adults with ASD. P. S. Powell^{*1}, M. R. Klinger¹, L. G. Klinger² and R. K. Kana³, (1)*University of North Carolina - Chapel Hill*, (2)*University of North Carolina*, (3)*University of Alabama at Birmingham*

Background:

The ability to use environment cues (i.e., context learning) to make sense of the world is an important cognitive skill. Previous studies examining implicit contextual learning in individuals with autism spectrum disorder (ASD) have reported mixed results (Barnes et al., 2008; Brown et al., 2010; Kourkoulou, et al., 2012; Powell et al., 2011). We hypothesize that, regardless of whether behavioral performance is intact, individuals with ASD may be using a more explicit rather than implicit learning approach. To date, there are no studies that have examined brain responses associated with a contextual cueing task in individuals with ASD.

Objectives:

The main goal of this fMRI study was to examine the neural circuitry underlying implicit contextual learning in ASD using a novel visual search task. We predicted that individuals with ASD would show less neural activation in areas typically associated with implicit learning.

Methods:

Fifteen high-functioning adolescents and young adults with ASD and 17 age and IQ-matched individuals with typical development completed a visual search task. Participants located a target Disney character (i.e., Jiminy Cricket) as quickly and accurately as possible while hidden amongst an array of 19 other distractor characters. Contextual information (the arrangement of the other 19 characters) predicted the location of the target. Participants had limited awareness that the arrangement of the characters predicted the location of the target. The data were collected on a 3 Tesla fMRI scanner. Before the MRI session, participants were given eight blocks of predictable trials to learn the contextual relations between characters. In the MRI scanner, the participants received a predictable block, an unpredictable block and a final predictable block of trials.

Results:

Current neuroimaging results are based on only six participants per group as analyses are ongoing. Individuals with ASD and individuals with TD demonstrated similar behavioral performance on the contextual cueing task. However, differences in neural activation emerged between the two groups. Individuals with ASD demonstrated lower levels of activation than individuals with typical development in the right precentral gyrus, right insula, left cerebellum, and left superior temporal gyrus ($p < .005$, uncorrected) during predictable trials. However, individuals with ASD demonstrated greater activation than individuals with typical development in the left caudate nucleus. Finally, across both predictable and unpredictable trials, individuals with ASD showed reduced activation in bilateral inferior parietal lobule (IPL) compared in individuals with typical development.

Conclusions:

Preliminary findings suggest that individuals with ASD demonstrate unique neural activation during a contextual cueing task compared to individuals with typical development. Greater activation of the left caudate during the predictable trials for individuals with ASD along with reduced activation in left and right IPL during both predictable and

unpredictable trials suggests that individuals with ASD have different activation of both implicit learning and strategic attentional areas of the brain compared to individuals with typical development.

108.169 169 Functional Connectivity of the Amygdala in 2- to 5-Year-Old Children with Autism Spectrum Disorder. M. D. Shen*, D. D. Li, R. T. Johnson, A. Lee, K. Angkustsiri, S. J. Rogers, D. G. Amaral and C. W. Nordahl, *University of California Davis Medical Center*

Background: The neuropathology of Autism Spectrum Disorder (ASD) likely involves abnormalities in white matter and neural connectivity patterns. Functional connectivity MRI during rest reflects spontaneous synchronous neural activity between distinct brain regions. Recent studies provide evidence for altered resting state functional connectivity in various brain networks in older children and adults with ASD, but studies in very young children are lacking. There is evidence from structural MRI studies for abnormal enlargement of the amygdala in young children with ASD; however, functional connectivity patterns of the amygdala in young children have not yet been assessed.

Objectives: We investigated resting state functional connectivity of the amygdala in 2- to 5-year-old children with ASD compared to typically developing peers (TYP).

Methods: We acquired high-resolution T1-weighted structural scans and resting-state EPI-BOLD scans during natural sleep in 64 male participants, aged 2-5 years (n=45 ASD, mean age 3.5 years; n=19 TYP, mean age 3.6 years). Participants were screened for medication use and excluded for any psychotropic medications. The left and right amygdala were manually traced according to an anatomically reliable protocol developed by our laboratory, and the resulting ROIs were used as seed regions for the functional connectivity analysis. Resting-state scans were pre-processed (time shifted, motion corrected, spatially smoothed, band-pass filtered) and aligned to the structural image in native individual space. The mean time-series of the left and right amygdala ROIs were extracted from each individual and correlated with all other voxels in the brain. Group comparisons were conducted in standard MNI space and significant clusters of

group difference were corrected for multiple comparisons at $p < .05$.

Results: Both diagnostic groups showed functional connectivity between the amygdala and several brain regions that are consistent with older healthy populations, including the striatum, inferior temporal cortex, visual cortex, and medial prefrontal cortex. However, direct group comparison revealed that the ASD group had reduced connectivity between the amygdala and multiple brain regions, with the greatest reductions in connectivity between the amygdala and anterior striatum and between the amygdala and visual cortex.

Conclusions: These findings suggest that the anatomical abnormalities found in the amygdala of individuals with ASD may be associated with altered functional connectivity of the amygdala in early childhood, particularly in brain regions that may underlie some of the sensory and behavioral features of ASD. Additional analyses will be conducted to examine the functional connectivity between the amygdala and other brain regions with known anatomical connectivity. We will also evaluate amygdala functional connectivity in previously identified phenotypic subgroups of ASD based on amygdala growth trajectories. Finally, we will evaluate whether functional connectivity between the amygdala and specific cortical regions is associated with behavioral symptoms of ASD.

108.170 170 Motor Cortex Functional Connectivity Signatures of Autism. M. B. Nebel*¹, A. Eloyan², A. D. Barber¹, B. S. Caffo², J. J. Pekar¹ and S. H. Mostofsky¹, (1)*Kennedy Krieger Institute*, (2)*Johns Hopkins Bloomberg School of Public Health*

Background: Motor impairments experienced by children with autism spectrum disorder (ASD) relate to the communicative/social deficits at the core of their diagnosis and may reflect abnormal connectivity within brain networks underlying motor control and learning. Resting state (rs) functional connectivity (FC) analysis is a potentially powerful tool to estimate brain organization within clinical populations like ASD but also poses challenges for quantitative image analysis, mainly related to the comparison of noisy signals from a large number of sources. Several groups have proposed parceling the brain prior to FC analysis to reduce the dimensionality

of the data and to enable rapid calculation of inter-parcel FC signatures for individuals.

Objectives: Motivated by these potentially scalable methods to investigate brain organization, the aim of this study was to estimate how well FC between subregions of the motor cortex (M1) discriminate individuals with ASD from typically developing (TD) participants.

Methods: rs-fMRI and anatomical images from the Autism Brain Imaging Data Exchange were used (368 ASD and 412 TD). Included participants were male, 6 to 40 years old and had a mean framewise displacement (between-volume motion) within two standard deviations of the sample mean. Data were adjusted for slice acquisition order and participant motion and normalized to MNI space using unified segmentation (SPM8). Nuisance covariates from white matter and CSF were estimated using CompCor and regressed from the data along with motion parameters, their derivatives, and global mean signal. Data were band-pass filtered (.01-0.1 Hz) and spatially smoothed (6-mm kernel).

The five-region M1 parcellation used to estimate FC signatures for each subject was derived from test-retest rs data from 20 TD adults and reflects the general organization of the motor homunculus. For each subject, correlations between the 10 pairs of mean parcel time courses were computed. Group differences were assessed using a multinomial logistic regression model. Demographic factors and M1 correlations were used as predictors, disease status as the outcome. To account for possible confounds among the many variables, generalized boosted methods were used to estimate model parameters. The spatial correlation between each subject's normalized data and SPM's EPI template was also included in the model to account for variability in the consistency of spatial normalization across subjects.

Results: Preliminary analysis suggests that IQ had a high relative influence in predicting disease status (35%) when all demographic variables and M1 parcel correlations were included. The correlation of the dorsomedial-most (DM) region, normally reserved for lower limb/trunk control, and the posterior lateral (PL) region (near the hand area) had the second highest relative

influence in the prediction model (24.6%). The third most influential factor also involved PL FC, but with the dorsolateral (DL)/upper limb region.

Conclusions: We identified potentially predictive FC signatures of ASD. FC disruptions between the DM/DL regions and the brain outside of M1 have been previously implicated in ASD. Here, we showed that FC between these regions and other parts of M1 (PL) may also be abnormal. These FC differences are consistent with deficits in complex multi-joint coordination associated with ASD.

108.171 171 Probabilistic Reinforcement Learning in Young Adults with Autism Spectrum Disorders Reflects Cognitive Control Deficits. M. Solomon*¹, M. J. Frank², A. C. Smith³, J. D. Ragland⁴, M. J. Minzenberg³, T. A. Niendam⁵, J. H. Yoon⁵, T. A. Lesh⁴ and C. S. Carter⁵, (1)Department of Psychiatry, MIND Institute, Imaging Research Center, (2)Brown University, (3)UC Davis, (4)Imaging Research Center, (5)UC Davis, Psychiatry

Background: Individuals with autism spectrum disorders (ASD) display a unique pattern of learning strengths and challenges. They show intact (or even enhanced) lower-level learning of stimulus response associations, of single items of information, of facts, of habits, and of information learned implicitly. However, they display deficits in *generalizing* (or transferring) 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: The goal of the current research is to illuminate the neural mechanisms of learning differences in persons with ASD using functional magnetic resonance neuroimaging (fMRI), and to translate findings into clinically relevant insights.

Methods: Participants included young adults aged 18-40 years with diagnosed with ASD, who were largely medication free and evaluated using gold standard diagnostic measures (n=22), and age, IQ, and gender matched young adults with typical development (TYP; n=25). They completed a probabilistic selection task where they were trained to choose the correct stimulus in three different stimulus pairs (AB, CD, EF) presented with feedback that was valid 80%, 70%, and 60% of the time, respectively. Participants had to

determine which was the rewarded stimulus from this relatively unpredictable feedback. Whole brain voxel-wise analyses were conducted using Bayesian state-space learning curves and prediction errors as parametric modulators. Regions of interest in the striatum, prefrontal cortex (PFC), and medial temporal lobes, were interrogated and functional connectivity analyses using these regions as seeds were conducted.

Results: As in our previous behavioral study, individuals with ASD learned the task to comparable rates as TYP, but were slower to learn. The ASD group exhibited greater striatal and medial temporal lobe activation during early learning that was related to task performance. There was less activation in prefrontal regions throughout learning in the ASD group, and unlike the TYP group, activation in the orbito-frontal cortex (OFC) was not related to the probability of having learned. Activation of the striatum during early learning was positively associated with restricted interests and repetitive behaviors in the ASD group.

Conclusions: Overall, results suggest that those with ASD have cognitive control related learning deficits. They use prefrontal brain regions including the OFC less, and rely on striatal, and medial temporal lobe regions to a greater extent, suggesting the use of these brain regions may be compensatory. Consequently they 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 goal directed behavior. There may be a relationship between repetitive behavior symptoms and their learning style. This interpretation is supported by the systems-level computational modeling work of Frank et al. (2004, 2005, 2006).

108.172 172 Relationships Between Resting State Neural Connectivity and Individual Differences in ASD Symptoms. G. K. Bartley*¹, A. N. Browne¹, J. D. Herrington² and R. T. Schultz¹, (1)*Children's Hospital of Philadelphia*, (2)*University of Pennsylvania*

Background:

Studies increasingly implicate neural short-range overconnectivity and long-range underconnectivity in the pathogenesis of autism. Research on resting state connectivity in autism has revealed

functional underconnectivity within and between resting state regions implicated in social processes, such as the medial temporal lobe and "salience" networks. However, the specificity of resting state network abnormalities and how they relate to the specific core symptoms and attributes of autism spectrum disorder (ASD) has yet to be fully established. In particular, the majority of resting state ASD studies to date have not benefitted from the large sample sizes needed to map connectivity networks onto individual differences in symptom profiles.

Objectives:

To examine and compare resting state networks between large samples of individuals with ASD and typically developing controls (TDC). Although our *a priori* hypotheses focus on default mode, "salience"/reward circuitry, and medial temporal lobe networks, a variety of cortical networks are considered. Dimensional (ASD symptom dimensions) and categorical (group) approaches to isolating abnormalities in resting state networks are used.

Methods: Participants in this study complete an extensive battery of psychodiagnostic and cognitive assessments (core ASD assessments include ADOS, ADI-R, Social Responsiveness Scale, and Social Communication Questionnaire). They also complete six minutes of resting state fMRI scanning (full head coverage, TR=2.340 ms). Data analysis follows three approaches. First, general linear model (GLM) examinations of connectivity are carried out on all gray matter voxels using *a priori* seeds within networks of interest. Second, spatio-temporal independent components analyses (ICA) are implemented to isolate resting state networks without *a priori* assumptions. Third, matrices of correlations between *a priori* brain areas are submitted graph theory-based analyses, including calculations of clustering coefficients, global and local efficiency. Each of these analyses yields statistics that are used as dependent variables in analyses on clinical variables (i.e., scores on the ADI, Social Communication Questionnaire, and Social Responsiveness Scale).

Results:

To date, resting state fMRI data have been collected from 45 participants with ASD (5 female) and 58 TDC participants (3 female) matched on age (TDC=11.5 years, ASD=11.3 years), and cognitive ability (Differential Abilities Scale GCA, TDC=109, ASD=105). Data collection for this project is ongoing, and will likely make this the largest single study reported to date on resting state functional connectivity in ASD.

Conclusions:

This study will provide preliminary results of selectivity of specific brain networks to ASD symptom profiles. They will also help determine optimal data analysis path (GLM, ICA, or graph theory) for identifying abnormal cortical networks in ASD. Ultimately, the identification of both global and local functional separations of components responsible for social processes, when measured as functions of ASD symptomatology, will refine our understanding of the relationships between structural/functional connections and core autism deficits.

108.173 173 Establishing fMRI Test-Retest Reliability:

Implications for fMRI Biomarkers of Treatment Efficacy. M. H. McDermott¹, A. N. Browne¹, L. Guy², J. D. Herrington¹ and R. T. Schultz*¹, (1)*Children's Hospital of Philadelphia*, (2)*The Children's Hospital of Philadelphia*

Background: Little is known about the reproducibility of fMRI data at the level of the individual person. Characterizing fMRI measurement reliability is important for studies that aim to use fMRI data to make individual level predictions, e.g., for studies that use fMRI to measure the effectiveness of an intervention, or to assess change across development. Unreliable measurements cannot successfully document meaningful changes that actually occur.

Objectives: To estimate the reliability of fMRI signals across time during a face recognition experiment over a 9-week interval in typically developing controls (TDC) and youth with an autism spectrum disorder (ASD).

Methods: Sixty-five participants (63 male) aged 12-17 (M= 14.78, SD= 1.66) participated in a study comprised of fMRI and behavioral markers at two time points separated by an interval of 9

weeks. Thirty-five participants had a diagnosis of ASD based on expert clinical diagnosis, ADOS and ADI-R scores. Thirty were recruited as TDCs. All participants were administered a block-design fMRI face-processing task consisting of 5 runs of both active (identity discrimination) and passive face viewing. Each run alternated between blocks of faces and blocks of houses requiring discrimination. Data were analyzed in FSL and with matlab scripts developed in our lab. Data analyses for 43 (29 ASD) of the 65 participants are presented here, with the remainder to be complete for the conference presentation.

Results: Interclass correlation coefficients (ICC) were computed for specific regions of interest (ROI) that were significantly active across groups at the whole brain level. Collapsing across groups, mean z scores within functionally defined ROIs (constrained within an anatomical search space) showed significant test-retest reliability for the fusiform gyrus (right: ICC=0.72, $p=0.000$; left: ICC=0.77, $p=0.000$) and the parahippocampal gyrus (right: ICC=0.86, $p=0.000$; left: ICC=0.79, $p=0.000$). However, mean signal from the amygdala did not show significant test-retest reliability.

Conclusions: Cortical regions that are face and house selective show robust test-retest reliability across the typical length of a medication trial with the stimuli, task design and other procedures used here. Thus, interventions that might target functional regions like these would be expected to show fMRI related signal change, should real neuronal level improvement occur with treatment. Notably, these preliminary data show better face-processing signal reliability for the medial fusiform gyrus, while group level contrasts of faces vs. houses show greater lateral fusiform activation, which is typical with the design of this study. Similarly, the group showed robust bilateral amygdala activation for the face vs. house contrast, but amygdala reliability was low and not significant in this portion of the total sample. Conference presentation will present the full data set and analyses that examine possible reasons for lower reliability in some regions (e.g., magnetic susceptibility artifacts at the interface of sinus and ear canals). We will also examine possible group differences in reliability and describe implications for using fMRI biomarkers in clinical translational research.

108.174 174 Brain-to-Brain Communication in Autism. G. Dumas*¹, E. Mercier², J. Martinerie¹, R. Soussignan³ and J. Nadel², (1)UPMC, (2)CNRS USR 3246, Centre Emotion, La Salpêtrière hospital, (3)CNRS UMR 517, CSGA

Background: Given the relationship between mu modulation and MNS activity, recent literature has started to provide results concerning mu modulation during observation compared to execution of action in ASD, and their link with social impairments. Results however remain controversial, due to the lack of a truly interactive design testing online the hypothesis of differential involvement of mu according to the nature of the stimuli observed, self-related versus other-related stimuli.

Objectives: In search of brain markers of social interaction, we have designed an innovative EEG hyperscanning platform associated to a live imitation paradigm. This design allows recording simultaneously the brain activities of pairs of subjects while they interact online through hand gestures. In a previous paper reporting the results of 18 subjects paired as 9 dyads, we have shown for the first time that an interbrain synchronizing network emerges in the alpha mu band between the right centroparietal regions when two subjects freely synchronize their gestures. So doing, we have extended to an inter-individual level the classical intra-individual comparison between brain activity during observation and execution of action.

Methods: Our design appears to allow such a test in a social context, stating that when individuals with ASD perceive to be synchronously imitated, they would modulate their mu and generate an inter-individual brain synchronization while they would not during the observation of another's own gesture. We have compared the behavioural and brain data of 40 volunteer subjects recorded as 10 pairs composed of a HF young adult diagnosed with ASD meeting a neurotypical young adult of the same gender, and 10 pairs of young neurotypical adults. Three tasks were presented (an observation task, an imitation of a pre-recorded video and a free imitation leading to behavioural synchrony) to explore how the alpha mu band responds to the design in High Functioning individuals with ASD and which are the conditions for the emergence of a synchronizing inter-brain network. A frame-by-

frame video analysis of the behavioural parameters allowed delineating the episodes of synchrony, imitation and be imitated for further brain analyses.

Results: Interbrain computation of oscillatory phenomena used cortical source reconstruction and coherence analysis. The presentation will focus on mu data during observation and free imitation tasks in the two kinds of dyads.

Conclusions: Discussion will include intra- and inter-individual levels.

108.175 175 A Comparison of Global Brain Volume, Regional Grey Matter and White Matter in Autism Spectrum Disorder and Its Relationship with Symptom Severity in Children and Adolescents: A Voxel-Based Morphometry Study. V. D'Almeida*¹, A. Shahidiani¹, E. Daly², L. Van-Hemert¹, N. Gillan¹, C. Ecker², D. Spain¹, M. Gudbrandsen³, S. C. Deoni⁴, S. C. Williams¹ and D. G. Murphy⁵, (1)King's College London, Institute of Psychiatry, (2)King's College London, Institute of Psychiatry, (3)Institute of Psychiatry, (4)Brown University, (5)Institute of Psychiatry. King's College London

Background: It has been widely reported that there are neuroanatomical differences in ASD. However, little consensus exists with regards to the regions implicated, in part due to the non-replication of findings. This may be because prior studies included individuals with co-morbid physical health problems and / or intellectual disability. As such, the exact neurobiological foundations of the highly variable behavioural phenotype of ASD are little understood.

Objectives: This study therefore aimed to investigate (a) if there are differences in global brain volumes between otherwise healthy children and adolescents with ASD and healthy controls of normal overall intelligence who did not significantly differ in gender, age and IQ; and (b) if volumetric differences are associated with clinical variation as measured by the Autism Diagnostic Interview-Revised (ADI-R) and the Autism Diagnostic Observation Schedule-Generic (ADOS-G).

Methods: Using non-invasive Magnetic Resonance Imaging (MRI) techniques, eighteen right-handed child and adolescent males with ASD (mean age =

12.5 (SD = 2.7); mean IQ = 105 (SD = 17.2)) and eighteen healthy controls (mean age = 13.9 (SD = 2.7; mean IQ = 108 (SD = 11.3)), who did not differ significantly in mean age and full scale IQ, were scanned at the Centre for Neuroimaging Sciences, Institute of Psychiatry, King's College London using GE 3 Tesla (T) MR system (General-Electric, Milwaukee, WI, USA). Voxel Based Morphometry (VBM) analysis was utilised to investigate the between group differences in neuroanatomy and to assess their relationship with ASD symptomatology as measured by the various domains in the ADI-R and ADOS-G using Pearson's product-moment correlation coefficient.

Results: Children and adolescents with ASD did not differ significantly from healthy controls in mean global brain volume, grey matter volume and white matter volume. There were however, significant volumetric differences in regional white matter between the two groups. White matter was predominantly reduced bilaterally in the internal capsule, and unilaterally in the left corpus callosum. Further, correlation analysis of regional differences indicated that white matter deficits in the internal capsule were correlated with severity of social and communication impairments.

Conclusions: Not all children and adolescents with ASD have macrocephaly. This may particularly apply to otherwise healthy individuals. Nevertheless, within this population differences in white matter development are associated with clinical variation.

108.176 176 A Two-Year Longitudinal Pilot MRI Study of the Brainstem in Autism. R. J. Jou^{*1}, T. W. Frazier², M. S. Keshavan³, N. J. Minshew⁴ and A. Y. Hardan⁵, (1)*Yale School of Medicine*, (2)*Cleveland Clinic Lerner College of Medicine*, (3)*Harvard Medical School*, (4)*University of Pittsburgh*, (5)*Stanford University School of Medicine*

Background: Research has demonstrated the potential role of the brainstem in the pathobiology of autism. Previous studies have suggested reductions in brainstem volume and the existence of a relationship between this structure and sensory abnormalities. However, very little is known regarding the developmental aspects of the brainstem across childhood and adolescence.

Objectives: The goal of this pilot study was to examine brainstem development via MRI volumetry using a longitudinal research design.

Methods: Subjects included 22 boys with autism and 22 gender- and aged-matched controls (age range = 7-17 years), all without intellectual disability. Structural MRI scans were obtained twice for each participant, once at baseline and again at two-year follow-up. Brainstem volumetric measurements were performed using the BRAINS2 software package.

Results: There were no significant differences in age and total brain volume between the two groups, but full-scale IQ was higher in controls. Autism and control groups showed different patterns of growth in brainstem volume. While whole brainstem volume remained relatively stable in controls over the two-year period, the autism group showed increases with age achieving normalization by age 15 years. This normalization of whole brainstem volume was primarily driven by increases in gray matter volume. These changes were similar across the left and right brainstem regions.

Conclusions: Findings from this study are suggestive of developmental brainstem abnormalities in autism primarily involving gray matter structures. These results are consistent with autism being a neurodevelopmental disorder with alterations in brain-growth trajectories. More longitudinal MRI studies are needed integrating longitudinal cognitive/behavioral data to elucidate the clinical significance of these atypical growth patterns.

108.177 177 Decreased Frontal Gyrfication Correlates with Altered Connectivity in Children with Autism. M. Schaer^{*}, S. Eliez, E. Scariati and B. Glaser, *University of Geneva Medical School*

Background:

Current clinical, cognitive and neuroimaging observations converge to propose two neurodevelopmental hypotheses in autism. A first hypothesis posits impairments in the maturation of the cerebral regions concerned with social competences, but detailed examinations of the nature of these changes (i.e. cortical thickness or gyrfication) are yet missing. A second hypothesis,

based on post-mortem and functional connectivity studies, postulates altered cerebral connectivity in autism. The structural counterpart of this functional dysconnectivity is however largely unknown.

Objectives:

Provide whole-brain measurements of cortical thickness (an index of brain maturation), cortical gyrification (a marker of early brain development), and structural connectivity using tractography in children with autism.

Methods:

We analyzed cerebral morphometry in a sample of 11 children with autism compared to their individually age- and gender-matched controls. This group consists of 8 male and 3 female children with autism, aged 9 to 15 years old, with an average IQ of 79.4 ± 18.1 . Cerebral MRI acquisitions included both anatomical T1-weighted images and Diffusion Tensor Images (DTI).

The T1-weighted images were processed using validated procedure embedded in *FreeSurfer* (<http://surfer.nmr.mgh.harvard.edu/fswiki>), yielding accurate measurements of regional cortical and white matter volumes. Cortical thickness and local Gyrification Index (GI, Schaer et al., 2008) were measured with an exquisite resolution across the cortex. All analyses covaried out the effect of age and gender and were corrected for multiple comparisons. To relate the cortical anatomy with the underlying architecture of white matter bundles, we used tools embedded in the Human Connectome (<http://www.connectomics.org/connectomemappe/r/>).

Results:

No between-group difference in cortical thickness was found. We observed 3 clusters with significant GI reduction in patients with autism as compared to controls, in the right inferior parietal region, the lower part of the precentral gyrus and the inferior frontal gyrus. Concomitantly with altered frontal gyrification, decreased volume was found in the

anterior part of the corpus callosum. Tracking the white matter fibers from cortical areas of significant gyrification difference, we observed significant positive correlations between the length of short-range connections and GI in patients with autism ($p < 0.001$), but not in controls.

Conclusions:

Reduced gyrification in the inferior fronto-parietal regions lends support for early-disrupted cortical growth in the fronto-parietal mirror neuron system, implicated in action imitation (Rizzolatti and Craighero, 2004). Early impaired neurodevelopment in the mirror-neurons system may alter embodied aspects of the self-others relationship in children with autism, providing initial substrate for altered maturation cascade of the cerebral networks responsible for more sophisticated social skills, such as empathy and theory of mind. We show that these gyrification abnormalities are further related to an imbalance of the short-to-long connectivity. Decreased volume of the anterior corpus callosum, connecting frontal hemispheres, points to reduced long-range connectivity in areas with reduced gyrification. Further, increased short-range connectivity was correlated with decreased cortical gyrification. Our results support the hypothesis that an imbalance between the short- and long-range connectivity, thought to impair high integration of information and coordination of multiple neural systems, also alters the shape of the brain of patients with autism during early stages of brain development.

109 Measuring Treatment Change in Core Symptoms: Novel Methods, Meaningful Outcomes

Moderators: L. B. Adamson¹C. Kasari² (1)Georgia State University, (2)University of California Los Angeles

Organizer: L. B. Adamson Georgia State University

A priority of the 2011 Interagency Autism Coordinating Council concerns 'Identifying methods for measuring changes in core symptoms of ASD from treatment'. The underlying issue is that we have few validated measures or methods to reliably assess change in core deficits that result from interventions. Currently outcome measures for treatments focus on standardized test results (IQ, language, adaptive behavior) or reports of behaviors by

parents or teachers that may indirectly assess the intervention targets. Change in core developmental difficulties are rarely assessed as an outcome of intervention; yet, they may be some of the most important measures of sustainable, meaningful change. This panel's main learning goals are to introduce new ways to measure meaningful treatment change and to provide compelling evidence of the sensitivity of these novel methods. To this end, researchers on this panel will describe advances in autism-focused assessment, observational methods, and computing technologies that can produce valuable information about meaningful treatment change. Data will be drawn from studies of core deficits in social communication, joint engagement, and social relations in populations that include infants and toddlers with autism, underserved children assessed in schools, and minimally verbal individuals with ASD and that focus on core symptom change.

109.001 Peer Social Skills and Social Relationships: Measuring Change in Real World School Settings. C. Kasari^{*1}, M. Kretzmann¹ and M. Dean², (1)*University of California Los Angeles*, (2)*University of California, Los Angeles*

Background: Social impairment may be the most complex and impenetrable core challenge facing children with autism. Not surprisingly the field has witnessed a significant increase in the number of intervention studies addressing social functioning. Most studies demonstrate improved outcomes based on children's tested social knowledge, and parental reported social skills. However, social functioning is rarely tested in environments (e.g., schools) that challenge the durability and depth of these intervention effects. Outcome measures remain limited with an over-reliance on potentially biased informants (i.e., involved in the intervention or unblinded). There is a critical need to develop reliable, objective measures of social functioning that can be measured in real world environments, and that measure changes that can be interpreted as meaningful and sustainable.

Objectives: To describe the application of social network methodology and social interaction observational measures collected in school environments. To determine if change measured over time provides an index of meaningful (generalizable, stable) change in child social functioning.

Methods: We have applied social network methods to children in school settings using an online data collection system that yields information on peer social connections, friendship reciprocity, and social status within the classroom social structures (the Friendship Survey). Peer social interactions during unstructured times during the school day (lunch, recess, transitions) have been assessed with live coding procedures yielding information on peer engagement, initiations and responses (Playground Observation of Peer Engagement-POPE). Data from nearly two hundred school- aged children with ASD (Kindergarten through fifth grade) have been assessed using these measures across multiple time points during the school year.

Results: We have found significant changes in social network status of children as a result of social skills interventions carried out at school in as little as 12 sessions, 6-weeks (Kasari et al, 2012; AIR-B in process). Data illustrating change in social network salience, friendship nominations and reciprocity will be presented for type of intervention that children receive as well as by gender and age/grade, and the stability of changes over time. POPEs coded during unstructured periods at school are also sensitive to change, and depend on the type of intervention applied (where intervention takes place, and who is delivering the intervention). The interconnectedness of these data will be presented to illustrate important considerations in their application to school settings, and for interpretation of 'real' social change.

Conclusions: Social network measures are easy to administer, and to code using online computerized programming. These measures are sensitive to change over short periods of time, and additionally can identify specific children who may be in need of interventions depending on their status within the classroom (e.g., isolated). The application of social network methods, and the additional observational data from playground observations can yield important data regarding children's real world social situations at school, the context in which children spend the most time every day. Limitations in these methods include when network data and observations do not match, and the potential challenges in obtaining informed consent to carry out these measures in school contexts.

109.002 Measuring Emerging Changes in Social Communication. C. Lord*¹, T. Carr² and R. Grzadzinski³, (1)*Weill Cornell Medical College*, (2)*University of Michigan*, (3)*Teachers College, Columbia University*

Background: Clinical trials testing the effectiveness of medical treatments on the behaviors of children with ASD have typically used parent questionnaires and clinician judgments heavily reliant on caregiver reports to measure outcomes. Using these measures, a number of approaches to decreasing behavior problems have been shown to be effective. Changes in response to behavioral clinical trials have typically been most evident for measures of general development and parent report measures of adaptive functioning. There has been much interest in measuring the effects of interventions on core features of autism. Several parent-report instruments have been proposed to fill these gaps. The advantage of observational measures, such as the ADOS, is that raters can remain truly blind to intervention status. However, though long-term changes in social-communication have been documented using calibrated scores from the Autism Diagnostic Observation Scale (ADOS), in general, the ADOS has not shown much effect of intervention. Other limitations include substantial correlations with verbal IQ; ADOS calibrated severity scores reduce these correlations, but result in children's scores being compared to other children of the same age and language level, which may underestimate the amount of change.

Objectives: To design and test a standardized observational method of measuring change in core features of ASD that can be used by different research projects employing different contexts for these observations and that allows independent, blind scoring of change in response to behavioral interventions.

Methods: The ADOS-C (ADOS-Change) provides a way of describing change in autism-specific social communication deficits. Standard 6 point codes for 15 social-communication behaviors are rated from a videotaped 10 minute interaction. Inter-rater and test-retest reliability have been established. Rather than contrasting scores of an individual child to normative scores from other children, the ADOS-C compares total scores of the same child in the same context at different times.

Multiple raters are currently coding data for over 100 children between the ages of 18 months to 3 years at at least three points: pre-intervention, post-intervention and follow-up from randomized controlled trials of three different early interventions and one multiple baseline study. These studies ranged greatly in length and intensity of treatment; all contexts were "natural" play during mother-child interactions.

Results: For several, but not all interventions, preliminary analyses of the ADOS-C showed changes when the ADOS did not. Illustrative data will be presented. Clinical validity of the measure was also tested by comparing scores from children nominated by therapists and those reported by parents as showing the least and greatest amount of change in behavior. Factors associated with changes were complex and have implications for research designs and for use of observational methods documenting changes in social-communication behaviors.

Conclusions: The potential to provide truly independent measures of more subtle changes in core features of ASD, as well as methodological issues for the ADOS-C and other measures of change in these features will be discussed, particularly in terms of planning and interpreting results of intervention studies.

109.003 Systematically Observing Changes in Joint Engagement During Parent-Child Interactions. L. B. Adamson*, R. Bakeman and D. L. Robins, *Georgia State University*

Background: Joint attention deficits characterize young children with ASD and motivate many early interventions. Although parent reports and experimenter-implemented assessments can measure joint attention skills, additional information about how these skills manifest during interactions is crucial for detailing treatment effects. Especially when intervention involve parents, it is essential to monitor not only changes in joint engagement but also in child and parent communicative acts and in shared topics.

Objectives: To develop a brief observational protocol to view parent-child communication that can efficiently produce reliable data about children's joint engagement and related aspects of social interaction for use in research, including

intervention studies, that monitors developmental trajectories.

Methods: The Communication Play Protocol (CPP) provides a stable frame for observing interactions by using the conceit of a Play to invite a parent (as supporting actor) to entice the child (the star) to enact scenes whose plots sample communicative functions including interacting, requesting, and commenting. To date, several hundred CPPs have been performed in studies that trace the typical developmental course of joint engagement, compare typical and atypical trajectories including those of young children with ASD, and assess the effect of early language interventions. Data have been extracted from videorecords using methods including state coding, language transcripts, and, most recently, validated rating items. Our current rating battery includes 16 items about forms of joint engagement (total, supported, coordinated, symbol-infused), child communicative acts (e.g., expressive language, initiating and responding to communication), parent actions (e.g., scaffolding, following child's focus, symbol highlighting), and topic characteristics (e.g., scope of shared topic).

Results: Drawing on our on-going large-scale longitudinal study of toddlers who screen positive for ASD on the M-CHAT-R, we document that the CPP rating items detail the pervasive effect of ASD on joint engagement. Screen-positive children subsequently diagnosed with ASD differ significantly from TD children on all items, and differ from screen-positive children who were not diagnosed with ASD on all child items except one (coordinated joint engagement) but on none of the parent items. Change over time is evident in significant differences on all items from pre-diagnosis (at on average 24 months) to a 6-month follow-up. Once trained, raters masked to child status generate reliable data quickly. But because the full CPP takes over 45 min to administer, we asked if a CPP with only 3 scenes, one each for interacting, requesting, and commenting, could produce the same results. It does, with correlations between versions uniformly high (96% above .80) and results related to group and age differences remaining essentially the same.

Conclusions : The CPP, even an abbreviated 15 min version, coupled with rating items generates

information about joint engagement and associated communication during parent-child interactions that is sensitive to diagnostic differences and change over time. Discussion includes consideration of applying the abbreviated CPP to monitor changes in interactions due to treatment, expanding the rating battery to include intervention-specific items, and using additional data capture procedures to gain more refined evidence related to the quality of low rate phenomena such as coordinated joint engagement.

109.004 Using Computational Tools to Measure Social Communication and Engagement in Young Children. G. D. Abowd*, A. Rozga, J. M. Rehg and M. Clements, *Georgia Institute of Technology*

Background: In light of recent advances in early screening and diagnosis of autism, there is a growing push for interventions targeting the early signs of autism. Many of these parent- and therapist-mediated interventions include a focus on social communication behavior and engagement as treatment targets, including social and joint attention, affective engagement, and nonverbal communication skills (e.g., Kasari et al., 2010; Carter et al., 2011; Casenhiser, Shanker, & Stieben, 2011; Kaale, Smith, & Sponheim, 2012). There is a clear need to develop reliable, objective measures of these skills to better assess the effectiveness of such early interventions and identify their active ingredients.

Objectives: To develop a suite of computational tools that will enable automated quantitative measures of key social communicative behaviors and engagement of young children engaged in dyadic social interactions.

Methods: We are collecting rich sensor data (high quality video and audio recordings, on-body sensing of electrodermal activity and movement) in toddlers aged 15-30 months engaged in a semi-structured play interaction with an adult examiner. The interaction itself consists of a series of presses for specific social communicative behaviors of interest. Data from seventy-four toddlers has been collected, with 24 participants assessed a second time approximately two months after their initial visit. We use the sensor data to develop computer algorithms to automatically detect and quantify individual social

communicative behaviors (e.g., attention to people and objects, smiling, gestures, vocalizations) and to predict ratings of the child's engagement in the interaction. We compare the performance of the automated measurement tools against human coding of these behaviors from video.

Results: Using commercially available software and hardware, as well as research prototypes, we have developed tools to automatically parse an interaction into its constituent parts, and to detect whether the child has made eye contact, smiled or vocalized within a given period of time. Using overhead cameras, we have developed algorithms to track the child and adult's heads and the objects involved in the interaction and to determine when a child directs attention to objects or to the examiner (or shifts gaze between the two) during the interaction. Using a camera worn by the examiner, we have developed algorithms to detect when a child makes direct eye contact with the examiner. Finally, we developed algorithms that use the child's speech/vocalization data to predict the examiner's ratings of the child's engagement in the interaction.

Conclusions: Our preliminary results suggest that it is possible to detect the building blocks of social engagement – visual attention, joint attention, affect, and vocalization – in an automated way using video and audio recordings. We believe these tools, if further developed, will enable researchers and clinicians to gather more objective repeatable measures of the treatment progress of children enrolled in early interventions, and to do it more efficiently at larger densities and time scales than current human-based observation and measurement.

Medical Co-Morbid Conditions Program 110 Medical and Emotional-Behavioral Comorbidity

110.001 Correlates of Parent-Reported SLEEP Problems in Preschool Children with Autism Spectrum Disorder. L. Zwaigenbaum^{*1}, I. M. Smith², P. Mirenda³, W. Roberts⁴, T. Vaillancourt⁵, J. A. Jivraj⁶, P. Szatmari⁷, S. Georgiades⁷, E. Duku⁷, A. Thompson⁷, S. E. Bryson⁸, E. Fombonne⁹, J. Volden¹ and C. Waddell¹⁰, (1)University of Alberta, (2)Dalhousie/IWK Health Centre,

(3)University of British Columbia, (4)University of Toronto, (5)University of Ottawa, (6)Department of Pediatrics, University of Alberta, (7)Offord Centre for Child Studies & McMaster University, (8)Dalhousie University/IWK Health Centre, (9)Montreal Children's Hospital, (10)Simon Fraser University

Background: Sleep problems are among the most common health-related problems associated with autism spectrum disorder (ASD) (Goldman et al., 2012), but little is known how sleep problems vary across the continuum of symptom severity and functioning in this population.

Objectives: To examine the relationships between sleep problems and phenotypic characteristics of preschool children with ASD (i.e., cognitive, language and adaptive skill level, ASD and comorbid emotional-behavioral symptoms), as well as parental stress.

Methods: Data were drawn from the *Pathways in ASD* study and included 363 preschoolers from five Canadian provinces, who were assessed within 4 months of diagnosis (mean age = 40.8 months, range 24-64 months). Parent-reported sleep concerns were assessed using the Children's Sleep Habits Questionnaire (CSHQ) total score. Other child characteristics were assessed using the Autism Diagnostic Observation Schedule (ADOS), the Merrill-Palmer-Revised Scales of Development (M-P-R), the Preschool Language Scale – 4 (PLS-4), the Vineland Adaptive Behavioral Scales-II (VABS-II) and the Child Behavior Checklist 1.5-5 (CBCL). Parents also completed the Parenting Stress Index-Short Form (PSI-SF). We examined whether age, sex and clinical features correlated with sleep concerns using Pearson r , followed by simple linear regression to examine the independent contributions of features showing positive correlations. We also examined the correlation between severity of sleep concerns and level of parental stress.

Results: Mean CSHQ total scores (44.9+8.4) were comparable to those reported in other preschool ASD cohorts (Goldman et al., 2012), with 224 of 363 (59.0%) scoring above the cut-point suggestive of clinically significant sleep problems (Owens et al., 2000). CSHQ total scores were not associated with sex ($t_{361}=.02$, $p=.99$), age ($r=.01$, $p=.80$), cognitive level indexed by the M-P-R ($r=-.07$, $p=.20$), nor language level on the

PLS-4 ($r=-.06$, $p=.28$), but were positively correlated with internalizing and externalizing symptoms on the CBCL ($r=.42$, $p<.001$ and $r=.43$, $p<.001$, respectively) and negatively correlated with ASD symptom severity on the ADOS ($r=-.11$, $p=.03$) and adaptive skills on the VABS-II ($r=-.11$, $p=.04$). The linear regression model that included the CBCL, ADOS and VABS-II accounted for 22% of the variance in CSHQ scores, with only the CBCL contributing unique variance (internalizing symptoms, $\beta=.24$, $p<.001$ and externalizing symptoms, $\beta=.25$, $p<.001$). CSHQ scores were also correlated with parental stress on the PSI-SF ($r=.33$, $p<.001$).

Conclusions: Parent-reported sleep problems were common across this large cohort of preschool children with ASD. Severity of sleep problems was significantly correlated with internalizing and externalizing symptoms (but not independently with ASD symptom severity nor cognitive/language levels) as well as parental stress. While the directionality of these relationships cannot be determined with cross-sectional data, recognizing that sleep problems, emotional-behavioral dysregulation and parental stress often co-occur may have important implications for both clinical surveillance and appropriate multi-faceted management. Future research with this longitudinal cohort will examine the reciprocal relationships between sleep problems, emotional-behavioral symptoms and parental stress over time, as well as the impact of interventions.

110.002 Clinical Characteristics of Children with Autism Spectrum Disorder and Co-Occurring Epilepsy. E. W. Viscidi^{*1}, M. F. Pescosolido¹, R. McLean¹, E. W. Triche¹, R. M. Joseph², S. J. Spence³ and E. M. Morrow¹, (1)*Brown University*, (2)*Boston University School of Medicine*, (3)*Children's Hospital Boston*

Background: The co-occurrence of autism spectrum disorder (ASD) and epilepsy is well known. The prevalence of epilepsy in ASD is frequently reported as 30%, yet has rarely been studied in large samples of individuals with contemporary ASD diagnoses. Associations have been reported between ASD and epilepsy and various characteristics such as female gender, lower cognitive ability, and developmental regression. However, findings have been inconsistent and often contradictory, which is likely due to inadequately powered sample sizes.

At present, there is insufficient information to make strong predictions as to which individuals with ASD are at greatest risk for epilepsy and what clinical characteristics are associated with the co-occurrence of epilepsy and ASD.

Objectives: To determine the prevalence of epilepsy and the clinical characteristics of children with ASD and epilepsy in a large patient population.

Methods: Cross-sectional study using four large cohorts of children with ASD for a total of 5,815 participants with ASD and 289 participants with co-occurring ASD and epilepsy. Children with and without epilepsy were compared on demographic and clinical characteristics. Multivariate logistic regression was used to examine the association between clinical characteristics and epilepsy.

Results: The prevalence of epilepsy in children with ASD age 2-17 years was 12.5%. In unadjusted analyses, epilepsy was associated with older age, female gender, lower cognitive ability, poorer adaptive and language functioning, and a history of developmental regression. After adjusting for IQ, age was the only characteristic that remained a significant predictor of epilepsy. In a multivariate model adjusting for all variables, age and cognitive ability were strongly and independently associated with epilepsy. Children age 10 or older had 1.61 times the odds of having epilepsy ($p <.001$), and for a one standard deviation increase in full scale IQ score, the odds of having epilepsy decreased by 48% ($p <.001$).

Conclusions: This is the largest study to date of clinical correlates in patients with ASD and co-occurring epilepsy. Based on a representative sample of children with ASD, the prevalence of epilepsy was approximately 12%, which is lower than previously reported. The proportion of epilepsy in ASD may be decreasing as the definition of ASD has expanded and the ability to detect cases has improved. Specifically, increases in the diagnosis of ASD in individuals of average or above-average IQ in recent years may have resulted in lower rates of epilepsy in the ASD population. Several clinical correlates of epilepsy were identified including female gender, low cognitive ability, poor adaptive and language functioning, and a history of developmental regression. Through statistical modeling we

demonstrated that several of the most-widely reported factors are not predictive after adjusting for IQ. These findings can help guide prognosis and alert clinicians to patients who are at increased risk for epilepsy.

110.003 Dimensions of Callous-Unemotional Traits in Autism Spectrum Disorder. S. R. Martins*¹, W. Mandy², D. H. Skuse³ and L. Roughan¹, (1)*Great Ormond Street Hospital NHS Foundation Trust*, (2)*Faculty of Brain Sciences, UCL*, (3)*Institute of Child Health, UCL*

Background: Recent attempts to understand the multifinality of Conduct Disorder (CD) in the general population of children with severe conduct problems has proven useful for developing effective treatments for CD and for developing clinically meaningful ways to subtype children with CD. Evidence suggests that children with severe behavioural problems can be subtyped according to; type of conduct problem (aggressive versus rule-breaking, and instrumental versus reactive aggression) and age of onset of CD (i.e. childhood versus adolescent onset CD). Recently however, a body of research has unearthed the prospect of subtyping CD by the presence of Callous-unemotional (CU) traits. Sub divisions of these traits have been divided into three domains, Callousness, Unemotional and Uncaring. Young people who have CD and CU traits tend to have earlier onset of conduct problems, more severe difficulties and worse prognosis. Little is understood about CU traits in children with autism spectrum disorder; however conduct problems are common in this population.

Objectives: To investigate how Callous-unemotional (CU) traits and Conduct Disorder (CD) present in a population of children with Autism Spectrum Disorder (ASD) and to examine whether the level of CU traits can put children with ASD at risk of more severe conduct problems, including conduct disorder.

Methods: Cross-sectional data were examined for 56 young people (84% male) with a clinical diagnosis of ASD. Parents completed a well-standardised parent-report interview (the 3Di) during the assessment to measure ASD, Oppositional Defiant Disorder (ODD) and CD symptoms. CU traits were measured using the Inventory of Callous-Unemotional Traits. Strengths and Difficulties Questionnaire by parent and teacher report

measured conduct and other behavioural problems.

Results: In children with ASD, Callous-unemotional traits were correlated with CD symptoms as reported by teachers ($r = .38$, $df = 50$, $p < .01$) and parents ($r = .42$, $df = 48$, $p < .01$). In a regression model with the total CU traits score as a predictor of CD symptoms; total CU traits were a significant predictor of CD symptoms by both parent ($\beta = .42$) and teacher ($\beta = .38$) report. Additionally, in a regression model with Callousness, Uncaring and Unemotional symptoms as predictors, only callous behaviour significantly predicted conduct problems by both parent ($\beta = .62$) and teacher ($\beta = .54$) report.

Conclusions: Callous-unemotional traits are important predictors in understanding conduct problems in an ASD sample. Of the three domains of CU traits, callous behaviour, appears to be an important construct in this population, and is associated with a specific risk factor for more serious conduct problems in ASD. By contrast, unemotional and uncaring behaviours do not seem to be significantly related to severity in conduct problems in children with ASD. Effective clinical assessment of CU traits in ASD populations may help identify children most at risk of developing more severe conduct problems and inform the development of appropriate intervention programmes for children with ASD.

110.004 Mental Health Difficulties in Toddlers At High-Risk for Autism Spectrum Disorders. K. N. Crea*¹, C. Dissanayake² and K. Hudry², (1)*Olga Tennison Autism Research Centre*, (2)*La Trobe University*

Background:

Mental health difficulties of childhood, including internalising problems such as anxiety, and externalising problems such as aggression, commonly occur in children with Autism Spectrum Disorders (ASDs). While siblings of children with ASDs may be at increased risk for similar difficulties, due to genetic and/or environmental risk factors, no research to date has explored this issue in young siblings under the age of 3 years.

Objectives:

This research extends existing findings by investigating mental health difficulties in 2-year-old siblings. Parent-reported mental health difficulties in toddlers at high genetic risk for ASD (by virtue of having an older sibling with an ASD diagnosis) were explored. The aim was to identify whether toddlers at high-risk for ASD presented increased risk or incidence of mental health difficulties compared with an age-matched low-risk control group.

Methods:

Participants were 30 two-year-old toddlers at high-risk for ASD, and 30 low-risk controls and their parents. Parents completed the 134-item Behavior Assessment System for Children, Second Edition (BASC-2; Reynolds & Kamphaus, 2004), Parent Rating Scales-Preschool form. The BASC results are broken down into three clinical composite/summary scales (e.g., overall Externalising problems) and eight clinical subscales (e.g., Anxiety).

Results:

Preliminary analysis across BASC composite scales suggests that toddlers at high-risk for ASDs present with more symptoms of Internalising Problems, Externalising Problems, and Behavioural Symptoms than do low-risk controls. Analysis of the BASC subscales indicates that toddlers at high-risk for ASDs are reported as having more symptoms of Hyperactivity, Aggression, and Depression. No differences were found between high- and low-risk toddlers on symptoms of Anxiety, Somatisation, Atypicality, Withdrawal, or Attention Problems.

Conclusions:

These results indicate that even two-year-old siblings of children with ASDs experience increased mental health difficulties compared with low-risk controls. These results are consistent with some of the literature for older-aged siblings of children with ASDs. Future analysis, including examination across 3-year diagnostic outcomes, will address the specificity of mental health difficulties in toddlers who do and do not go on to an ASD diagnosis, themselves.

110.005 The Utility of Psychophysiological Approaches in Assessing the Validity of Co-Morbid Anxiety in Autism Spectrum Disorders. L. Sterling*¹, P. Renno², G. Dawson³ and J. J. Wood⁴, (1)UCLA Semel Institute for Neuroscience & Human Behavior, (2)UCLA, (3)Autism Speaks, UNC Chapel Hill, (4)University of California Los Angeles

Background: According to the literature, individuals with autism spectrum disorders (ASD) experience high rates of comorbid psychopathology, particularly anxiety disorders. No validated measures of associated psychiatric symptoms exist for the ASD population. Psychophysiological approaches offer promise for differentiating symptoms of anxiety from core autism symptoms among individuals with ASD.

Objectives: To describe potentially useful psychophysiological approaches for detecting anxiety in youth with ASD. Data from two studies piloting reliable physiological measures of anxiety with youth with ASD will be presented. One approach, startle response, will be discussed given its relation to amygdala function and implications for the pathogenesis of both autism and anxiety.

Methods: In Study 1, 20 high-functioning adolescents with ASD and 19 typically developing (TD) adolescents participated in a fear potentiated startle (FPS) paradigm. Measures of social (Social Skills Rating Scale; Social Responsiveness Scale) and psychiatric (Revised Children's Manifest Anxiety Scale; RCMAS and Child Behavior Checklist; CBCL) symptoms were administered to teens and their parents; eyeblink magnitude and latency (electromyographic activity; EMG) was measured during the FPS paradigm. In Study 2, twenty participants with ASD, ages 7-14, have completed a startle paradigm, during which EMG, skin conductance, and heart rate is collected. Participants also complete measures of anxiety (e.g., Pediatric Anxiety Rating Scale; PARS and Multidimensional Anxiety Scale for Children; MASC).

Results: In Study 1, parents of teens with ASD reported significantly higher rates of associated psychopathology compared to TD peers (CBCL Internalizing: $t(35) = 8.19, p < .001$; CBCL Anxious/Depressed: $t(35) = 4.17, p < .001$). Both groups demonstrated normal potentiated startle response, evidenced by larger response to the Threat versus Safe condition ($t(893) = 5.80, p < .001$). Social impairment was unrelated to startle

response. In Study 2, convergent validity was examined through testing the association between physiological arousal and manifest anxiety symptoms; preliminary findings indicate that baseline skin conductance is significantly related to a total score on the PARS (Overall Severity of Avoidance of Anxiety-Provoking situations; $r(7) = .688, p < .05$), and marginally correlated with the MASC Somatic/Autonomic parent rating ($r(10) = .536, p = .072$). Convergent validity between heart rate, EMG, and behavioral measures of anxiety will also be examined in a larger group of children expected to be enrolled within the next 5 months ($N = 40$).

Conclusions: Results indicate that individuals with ASD demonstrate normal startle response, suggesting this aspect of amygdala function is intact (and unrelated to social deficits associated with ASD). Further, physiological reactivity may be related to manifest anxiety symptoms, which mirrors patterns observed in the TD population. These results support the notion that anxiety symptoms in youth with ASD are mediated by analogous physiological mechanisms as those observed in TD children; as such, a subset of individuals on the autism spectrum may experience anxiety as symptoms that are distinct from core ASD symptoms. Additional approaches, including examination of cortisol levels for participants in Study 2, will be presented as potential approaches for further differentiating anxiety from core symptoms in ASD.

110.006 Urinary p-Cresol in Autism Spectrum Disorder. A. M. Persico*, *University Campus Bio-Medico*

Background: Autism is a neurodevelopmental disorder, yet the elevated incidence of immune abnormalities, gastrointestinal (GI) symptoms, macrosomy, as well as peripheral markers of disease such as elevated 5-HT blood levels underscore that autism is a systemic disease. We found significantly elevated urinary amounts of p-cresol (4-methylphenol) in autistic children up until 8 years of age. P-cresol can be absorbed through the skin, GI or respiratory tracts, but its main source is represented by some gut bacteria including several clostridia, which express synthetic enzymes able to push the fermentation of tyrosine up to the formation of p-cresol.

Objectives: (1) To measure urinary amounts of total p-cresol and of its components p-cresylsulphate, p-cresylglucuronate and free p-cresol, in an independent sample of French autistic children and controls, while assessing also correlations with autism severity; (2) to study the behavioral effects of acute p-cresol administration in BTBR mice; (3) to investigate the origin of elevated urinary p-cresol in small autistic children.

Methods: (1) Recruitment of 34 French children ($N=17$ ASD and 17 matched controls, final $N=25$ each) and psychodiagnostic battery; measurement of total p-cresol and components using HPLC-ultraviolet diode array detection; (2) Acute i.v. injection of twelve male BTBR mice at P60 with p-cresol 1 mg/Kg ($N=4$), 10 mg/Kg ($N=4$), or vehicle ($N=4$) and behavioural assessment in the open field, elevated plus maze and object recognition test; (3) parallel assessment of urinary p-cresol, intestinal permeability using the LA/MA test, presence of Clostridial species in the feces as well as toxinA and calprotectin, stool habits and recent antibiotic use in 41 Italian ASD children and 16 controls.

Results: (1) urinary p-cresol is significantly higher among French ASD cases compared to controls ($p<0.05$), only prior to age 8 ($P<0.01$) and with a significant positive correlation with clinical severity; (2) acute p-cresol largely increases time spent in the open arms of the plus maze and decreases exploration of novel objects at the object recognition test ($P<0.05$ or 0.01), with no effect in the open field; (3) elevated urinary p-cresol does not appear associated with enhanced gut permeability, constipation or presence/titre of fecal Clostridial species, whereas there appears to be an association with recurrent ear infections and recent antibiotic use.

Conclusions: These preliminary studies replicate and largely extend our initial findings (Altieri et al., *Biomarkers* 16:252-260, 2011), showing that p-cresol is elevated in a substantial group of small autistic children, it is correlated with more severe autistic behaviors, it is behaviorally active in BTBR mice, and may possibly stem from frequent antibiotic use in part due to recurrent ear infections. If confirmed, they will support the testing of probiotics designed using cresol-resistant species in small autistic children with elevated urinary p-cresol. Furthermore, they will

strengthen initial converging evidence pointing toward possible roles for postnatal environmental factors in modulating the severity of ASD, while not causing the disease.

110.007 Emotion Regulation: Relations with Socio-Emotional Adjustment in Preschoolers with Autism Spectrum Disorders and Typically Developing Peers. N. M. Reyes* and A. Scarpa, *Virginia Tech*

Background: Previous research has widely reported that children with autism spectrum disorders (ASD) show poor social competence (Dawson & Faja, 2008); however, little is known about their emotional development (Begeer, Koot, Rieffe, Meerum Terwogt, & Stegge, 2008), which might be closely related to their social development (Halberstadt, Dunsmore, & Denham, 2001).

Objectives: Thus, the goal of this ongoing research study was to examine associations among emotion regulation, emotionality, and display of positive and negative affect with social skills and prosocial behaviors in children with High Functioning Autism (HFA) and typically developing (TD) children.

Methods: In this cross-sectional study, 22 preschoolers participated in a comprehensive evaluation to assess their social, emotional, autism symptoms, and cognitive abilities. The Emotion Regulation Checklist, Emotion Regulation Questionnaire, Children Reaction Questionnaire, Strengths and Difficulties Questionnaire, Vineland Adaptive Behavior Scales, Second Edition, the Autism Diagnostic Observation Scale (ADOS), and the Peabody Picture Vocabulary Test, Fourth Edition (PPVT™-4) were used to assess 12 TD children (*M* chronological=46.08 mo.) and 10 children with ASD (*M* chronological age=69.29 mo.).

Results: First, in children with ASD, emotion regulation was associated with positive emotional reactions, social reciprocity, play and leisure skills, and coping skills. Nonetheless, in typically developing children, emotion regulation was only associated with positive emotional reactions and prosocial behaviors. Second, less emotion regulation competence was linked to increased emotionality and negative emotional reactions in children with ASD. However, less emotion

regulation competence was only associated with increased behavioral problems in TD children. Further, emotionality was related to sadness and negative emotional reactions in the ASD group, but only to sadness in the TD group. Regarding display of emotions, positive emotions were linked to prosocial behaviors and social reciprocity in children with ASD, but only to social difficulties in children with typical development. Interesting, sadness was positively associated with prosocial behaviors and social reciprocity in children with ASD. Positive emotional reactivity was also associated with social reciprocity, play and leisure, and coping skills in TD children, but negatively related to social reciprocity in the ASD group. Further, emotional difficulties were positively related to behavioral problems and social difficulties in the ASD group. Notably, prosocial behaviors were associated with social reciprocity, play and leisure, and coping skills in both groups.

Conclusions: Preliminary results from this ongoing research project indicate that emotion regulation competence, emotionality, and display of affect are associated with social skills and prosocial behaviors in children with ASD and typical development. However, significant differences in socio-emotional correlates of emotion regulation also emerged between the groups. This is the first study that attempts to examine socio-emotional profiles in children with ASD, which can potentially inform the development and improvement of interventions addressing solely social skills difficulties.

110.008 Prevalence of and Associations with Co-Morbid Psychiatric Symptoms in Children with ASD in an Urban Elementary School District. A. S. Nahmias*¹ and D. S. Mandell², (1)*University of Pennsylvania*, (2)*Perelman School of Medicine at the University of Pennsylvania*

Background: The reported prevalence rates of co-occurring psychiatric symptoms and disorders in children with autism spectrum disorders (ASD) has varied widely. Relatively little research has investigated these rates in ethnically diverse community samples. Previous research findings differ as to whether associations exist between psychiatric symptoms and other characteristics of children with ASD, such as autism severity, IQ, age, gender, and ethnicity (Gadow et al., 2005; Gadow et al., 2008; Lecavalier, 2006; Simonoff et al., 2008).

Objectives: 1) to examine the prevalence of co-morbid psychiatric symptoms in an urban community sample of children with ASD; and 2) to examine the associations among child characteristics and co-morbid psychiatric symptom severity in this sample.

Methods: Children in kindergarten-to-second grade autism support classrooms in the School District of Philadelphia were administered the Differential Abilities Scale-2 (DAS) and Autism Diagnostic Observation Schedule (ADOS). Parents completed the Child Symptom Inventory-4 (CSI), a standardized measure of the severity of DSM-IV psychiatric symptoms. On average the 182 boys and 30 girls were 6.5 (SD=.9) years old, had DAS general conceptual ability scores of 60.8 (SD=20.3), and ADOS severity scores of 6.4 (SD=2.0). The sample had the following ethnic breakdown: 46.2% black, 23.6% Caucasian, 10.4% Hispanic/Latino, 5.7% Asian, 4.2% multi-ethnic, and 9.9% unknown. Semi-partial correlations (*sr*) were calculated to investigate the association between symptom severity scores and child characteristics while controlling for the other predictors. Effects sizes were interpreted based on *r* (small=.1, medium=.3, large=.5).

Results: Based on the CSI, 64.6% of participants exhibited psychiatric symptoms in the severe range (t-score >70; >98th percentile) in at least one of the following DSM-IV symptom categories: ADHD Inattentive (I), ADHD hyperactive-impulsive (HI), ADHD-combined (C), oppositional defiant disorder (ODD), conduct disorder (CD), generalized anxiety disorder (GAD), social phobia (SP), separation anxiety (SA), major depressive disorder (MDD), and dysthymic disorder. The most common symptom category for which children demonstrated clinically significant symptoms was SP (38.7%), followed by ADHD-HI (26.4%), ADHD-C (25.8%), ADHD-I (21.7%), ODD (24.1%), MDD (10.4%), SA (9.4%), dysthymic disorder (8.5%), and CD (8.5%). The associations between psychiatric symptom severity and other child characteristics differed for each of the symptom categories. Higher autism symptom severity was associated with lower ODD (*sr*=.2), dysthymic (*sr*=.2), and SP (*sr*=.1) severity. IQ had a negative association with ADHD-I (*sr*=.3). Younger age was associated with higher ADHD-I, ADHD-HI, ADHD-C and lower CD severity scores (*sr* =.2). Girls had higher CD,

dysthymic, SP, and SA severity scores than boys (*sr*=.2-.3). Ethnicity differences in symptom severity also emerged. Black children had lower GAD scores than Caucasian children (*sr*=.1). Hispanic children had higher MDD scores than black children (*sr*=.2) and higher dysthymic scores than the other children. All results were significant at *p* < .05.

Conclusions: Clinically significant symptoms of ADHD, anxiety, disruptive behavior, and mood disorders are present in many children with ASD, and should be important considerations in treatment planning. The associations among these symptoms and autism severity, IQ, age, gender, and ethnicity may have implications for understanding of the role of co-morbid psychiatric symptoms in ASD.

Clinical Phenotype Program

111 Screening and Diagnosis

Moderators: J. A. Vorstman¹C. M. Freitag² (1)Brain Centre Rudolf Magnus, (2)Goethe University

This session focuses on recent advances behavioural screening and discoveries leading towards possible molecular biomarkers. Consideration is given to the factors that influence both detection and clinical diagnosis in a range of clinical groups from infancy to adulthood.

111.001 Specificity of the Social Responsiveness Scale When Used with Children with Other Diagnoses. V. Hus*¹, S. L. Bishop² and C. Lord². (1)University of Michigan, (2)Weill Cornell Medical College

Background: Child characteristics not specific to Autism Spectrum Disorders (ASD), such as behavior problems and IQ, have been shown to influence scores on ASD screening instruments in children with ASD (e.g., Corsello et al., 2007; Hus et al., 2012). Studies examining whether child characteristics affect screening measure scores in children with non-ASD diagnoses have been limited to relatively small, heterogeneous samples (e.g., Charman et al., 2007; Warren et al., 2011). Non-ASD-specific influences on ASD screeners may contribute to false positives that result in inappropriate referrals to specialty ASD clinics when used in clinical settings and erroneous inclusion of children with non-ASD diagnoses in research studies.

Objectives: To explore relationships between non-ASD-specific child characteristics and scores

on the Social Responsiveness Scale (SRS; Constantino & Gruber, 2005), a widely used parent-completed ASD screening questionnaire, in a sample of children with non-ASD diagnoses.

Methods: Participants were 161 children with non-ASD diagnoses recruited for a research study. Clinicians blind to previous diagnoses made clinical diagnoses based on information from comprehensive assessments for ASD including questionnaires, the ADI-R, Vineland-II, ADOS and cognitive testing. Diagnoses were grouped into: Intellectual Disability, Anxiety Disorders, ADHD, Language Disorders and Other. Using these clinician diagnoses as the "gold standard," specificity for the overall sample and individual diagnostic groups was calculated for T-score (60 or 76) and raw score (65 for females/70 for males or 85 for both) cut-offs recommended by the SRS authors for use in different settings. T-Tests were used to compare characteristics of children who did and did not meet cut-offs. Logistic regression was used to determine best predictors of meeting SRS cut-offs; binary predictors grouping children according to common divisions of standard scores (below average/average; borderline to clinical range of concern/normal) were used to compute odds ratios.

Results: Overall specificity ranged from 29-70%. Specificity was lowest when using the ASD cut-off (raw score=65/70) recommended for general population screening and for groups with Intellectual Disability, ADHD, or Other diagnoses. Children meeting cut-offs had more impaired social and expressive communication skills on the Vineland-II, more behavior problems on the Child Behavior Checklist, and lower IQ ($p < .001$) than children who did not meet cut-offs. For children with Internalizing or Externalizing scores in the borderline/clinical range, the odds of meeting the cut-off was 5.46 and 3.52 times the odds of children in the "normal" range. Post-hoc analyses indicated that scores in the borderline/clinical range on the Anxious-Depressed, Withdrawn-Depressed, Attention Problems, or Syndrome Scale significantly predicted meeting the ASD cut-off on the SRS (odds ratios of 5.53, 4.64 and 3.58, respectively).

Conclusions: Consistent with previous reports in ASD samples, non-ASD-specific characteristics, particularly behavior problems, have considerable

effects on SRS scores in non-ASD samples and reduce specificity of this screening instrument. Clinicians and researchers should exercise caution when using the SRS as a screening instrument in populations of children with elevated emotional and behavioral difficulties. Results will be further discussed for different diagnostic groups and from the perspective of using the SRS as a dimensional measure of ASD-related symptoms or social-communication impairments.

111.002 Development of a Culture Appropriate Screening Tool (NDST) for Detecting Neuro-Developmental Disorders in Children in the Community. A. Mohapatra*¹, V. B. Deshmukh¹, M. Nair², S. Gulati³, V. K. Bhutani⁴, D. H. Silberberg⁵, N. K. Arora¹ and I. Group⁶, (1)*The INCLEN Trust International*, (2)*Medical College*, (3)*All India Institute of Medical Sciences*, (4)*Stanford University School of Medicine and Lucile Packard Children's Hospital*, (5)*University of Pennsylvania Medical Center*, (6)*The INCLEN NDD Study Group, The INCLEN Trust International*

Background: There is a need to develop locally available tools to efficiently screen for the neuro-developmental disorders (NDDs) in children from resource constrained communities.

Objectives: To develop a culture and linguistically appropriate neuro-developmental disorders screening tool (NDST) for ten NDDs in children aged 2-9 years; and to validate and test field application at five sites across India.

Methods: *Development of NDST:* The 39 questions NDST was developed in English based on the *ten questions questionnaire* (TQ) to screen for a larger number of NDDs. It was translated to vernacular language and piloted on 593 subjects (325 children with confirmed diagnosis of NDD and 268 with no NDD, aged 2-9 years) identified from outpatient/specialty clinics of nine participating medical institutions located in different parts of India. Piloting revealed that the content validity of individual item and item-clusters, contextual meaning and relevance of examples were not always clear in every region. Several questions lost their essence and content due to lack of suitable equivalents in Indian languages after translation from English phrases. The questions needed re-sequencing as clustering of disability specific items invited biased response. Consequently, the instrument was re-discussed, modified and reframed in Hindi and re-sequenced. This version of NDST was translated to English.

Both English and Hindi versions were shared with site investigators for translation into respective vernacular languages. The modified NDST retained cultural flavor, was easy for paramedical staff across the country to administer, and for parents to understand. The NDST was subjected to reliability tests (test re-test and inter-rater) at two sites (New Delhi and Thiruvananthapuram). The test-retest reliability was measured by Spearman-Brown split-half reliability coefficient and the inter-rater reliability through intra-class correlation coefficient. Test re-test reliability coefficient was above 0.8 for 35 (89.7%) questions for both doctors and research assistants. Inter-rater reliability correlation coefficient was above 0.8 for 21 (53.8%) questions; no item had a reliability coefficient less than 0.5. No item during test-retest reliability assessment and three items in the inter-rater reliability test were in the 0.5-0.6 range at both sites. Overall, the NDST was performing similarly in New Delhi and Thiruvananthapuram and between doctors and research assistants. *Validation:* Subsequently, NDST has been applied in the field on 4000 children (2-9 years age) selected from five regions using population proportionate to size cluster sampling technique (200 clusters of 20 children – five boys and five girls in each of 24-71 and 72-107 months age group), separately by a field assistant and a doctor, on the same child and validated against the consensus clinical criteria diagnoses.

Results: Preliminary analyses from the sites suggest a sensitivity and specificity of NDST above 90% when the field assistant administered the instrument. The specificity increased further by 3.5% when NDST was applied by the doctor on the screen positives. Analysis is ongoing and the detailed results shall be presented.

Conclusions: This experience of constructing a culture appropriate tool may be extended to other LMICs.

111.003 Clinical Assessment of ASD in Adults Using Self and Other Report: Psychometric Properties and Validity of the Adult Social Behavior Questionnaire (ASBQ). E. H. Horwitz*¹, R. A. Schoevers¹, R. B. Minderaa², D. Wiersma¹ and C. A. Hartman³, (1)University Medical Center Groningen, (2)University of Groningen and University Medical Center Groningen, (3)University of Groningen, University Medical Center Groningen

Background:

Psychometrically sound questionnaires measuring adult autism spectrum disorders (ASD) are scarce but much-needed for 1) epidemiological research, 2) measurement of subthreshold ASD problems, and for 3) profiling scores on different ASD problem domains in patients with a formal ASD diagnosis.

Objectives:

The aim of this study is to develop a multidimensional ASD questionnaire reflecting the heterogeneous nature of the disorder and the multiple problem domains that can be discerned. Our aim was further to measure both the patient's perspective and that of an important other (a parent or a spouse) for a comprehensive picture of the ASD problems. Without compromising on psychometric quality, we additionally aimed for a brief questionnaire for practical usefulness.

Methods:

We built on our previous work on the Children's Social Behavior Questionnaire which we developed for children and adolescents (CSBQ; Hartman *et al.* 2006), formulating multiple adult (developmentally appropriate) equivalents of the CSBQ behaviors in a self-rating and other-rating version. A comprehensive item pool was subjected to principal component analysis. Items were selected with a factor loading $>.3$ on its main factor and a minimum difference of $.2$ with a possible secondary factor. These requirements had to apply to both the self- and other-report data. Findings are based on 1143 self-report and 644 other-report questionnaires from 6 outpatient clinics in the Netherlands. Ratings of patients and their proxies from different diagnostic groups were compared to determine criterion validity.

Results:

Principal Component Analyses yielded a, highly comparable, six factor structure in both the self- and other-report data. A total of 42 items (6-7 items per factor) fulfilled aforementioned criteria, 38 items being present in both versions and the remaining 3 items informant specific. The content of the subscales was similar to the subscales of

the CSBQ. Internal consistency of the total and the subscales and correlations between self- and other-ratings were good. Score profiles from self- and other report for the ASD group differentiated from those from the other patient groups.

Conclusions:

We developed a self- and other-report questionnaire of adult ASD problems which differentiates between the following domains: reduced contact, reduced empathy, reduced interpersonal insight, violation of social conventions, insistence of sameness, and sensory stimulation/motor stereotypies. The instrument, the Autism Social Behavior Questionnaire (ASBQ) is short, easy to apply, has satisfactory psychometric qualities and yields a score profile among these six problem domains both from the perspective of the patient and from someone close. Total score and score profile on the ASBQ differentiated a group with ASD from clinical control groups and yields a differentiated picture of this heterogeneous condition.

111.004 Can Internal Metrics of Reporting Bias Enhance Early Screening Measures?. C. M. Taylor*¹, A. Vehorn², H. Noble², J. A. Crittendon¹, W. A. Loring², C. R. Newsom², A. Nicholson² and Z. Warren¹, (1)Vanderbilt Kennedy Center, (2)Vanderbilt University

Background: The use of screening tools to identify children at risk for an Autism Spectrum Disorder (ASD) is recommended by numerous practice organizations including the American Academy of Pediatrics (Johnson & Meyer, 2007). The Modified Checklist for Autism in Toddlers [M-CHAT] (Robins et al., 2001) is one of the most widely-used screeners. Despite wide use and building data suggesting the ability of this instrument to capture many children at risk for ASD, concerns remain regarding the sensitivity and specificity of the M-CHAT in certain contexts (Zwiagenbaum, 2011). Specifically, research on parent reported ASD instruments at later ages has been demonstrated to relate to non-specific ASD behavioral concerns (Warren et al., 2012) and parenting stress (Weitlauf et al., 2012). Thus, the psychometric value of ASD screening instruments may be impacted by reporting characteristics or response biases. If so, internal metrics indicating potential reporting concerns (e.g., validity questions indicating over- or under-reporting patterns) that are used on many other self-report

instruments (e.g., MMPI) may aid early screening initiatives.

Objectives: The goal of this study was to examine the potential value of validity questions (divided into faking-good/under-reporting and faking-bad/over-reporting categories) to improve accurate identification of children at risk for ASD with the M-CHAT.

Methods: Participants in the study were caregivers of children (n=145), 36 months of age or younger participating in first-time diagnostic appointments across our clinical research center. Caregivers were asked to fill out an M-CHAT as well as an additional questionnaire containing six response pattern/validity questions. Validity questions, pulled from other parent report screening instruments, included items that most parents answer in the same way, regardless of child diagnosis. Clinical diagnosis of the children was made by a research-reliable, licensed clinician with a specialty focus in autism. Diagnostic assessment included clinical interview, cognitive assessment, adaptive behavior assessment, and information from the Autism Diagnostic Observation Schedule (ADOS; Lord et al., 2000). As a result of the evaluation, eighty-six children were diagnosed with an ASD and fifty-nine children were not given an ASD diagnosis.

Results: Eighteen children were identified as typically developing, all of whom passed the M-CHAT. Of the eighty-six children diagnosed with an ASD, 14% (n=12) passed the M-CHAT (false negative). Forty-one children received a developmental diagnosis other than ASD. Sixty-three percent (n=26) of these children who received an alternate developmental diagnosis failed the M-CHAT (false positive). When faking-good questions were taken into account, false negatives within the ASD sample decreased by 50%. When faking-bad questions were taken into account, false positives within the other developmental diagnosis sample decreased by 34%.

Conclusions: The addition of validity items significantly decreased false positives and false negatives in toddlers participating in assessment for autism. While screeners are useful to identify children who may have autism, there are still concerns about the sensitivity and specificity of

these measures. In the future, we should consider adding validity questions to ASD screeners to identify parents who may be over- or under-reporting symptoms.

111.005 Moving towards Rapid and Mobile Detection of Autism. D. Wall*, *Harvard Medical School*

Background: The incidence of autism has increased dramatically over recent years, making this mental disorder one of the greatest public health challenges of our time. The standard practice of diagnosis is based on behavioral characteristics, as the genome has largely proved intractable for diagnostic purposes. Yet, the most commonly used behavioral instruments take up to 3 hours to administer by a trained specialist, contributing to the substantial delays in diagnosis experienced by many children, who may go undiagnosed and untreated until ages beyond when behavioral therapy would have had more fundamental positive impacts. In an effort to mitigate these challenges, we have developed a machine-learning based system for classification of autism that requires minutes to administer and that can be delivered via mobile technologies.

Objectives: Our objectives in this study were threefold: (1) To prospectively validate the sensitivity and specificity of a rapid and mobilized method for detection of the core features of autism that combines home video with a parent-assessment report. (2) To assess the feasibility of obtaining parent recorded home videos of quality and content sufficient to detect behaviors consistent with an ASD diagnosis. And, (3) to detect the value of rapid, pre-clinical assessment of ASD for improving patient management at clinical sites.

Methods: We use machine learning techniques to analyze a large collection of archived score sheets from two of the most commonly used behavioral instruments, the Autism Diagnostic Interview-Revised (ADI-R) and the Autism Diagnostic Observation Schedule (ADOS), in an effort to identify a small subset of behavioral classes that have most value in detection of children with autism. We then applied the resulting behavioral

classifiers to over 5000 independent score sheets and several hundred home videos from children both with and without clinical diagnoses of autism to measure the sensitivity and specificity of the classification system overall. Next we administered and tested this system prospectively in a sample of over 100 children to clinically validate the utility of the classification tool and its potential value for patient triage.

Results: Our classification approach matched the outcomes of the standard instruments in 97% of all autism and 92% of all non-autism cases, including a set of cases with learning delay and clinically challenging symptom presentation. Our results confirm that rapid analysis of home videos strengthens the confidence in classification, and that the method of video scoring can scale to match the size of the risk population. Finally our results demonstrate that pre-clinical screening through a mobilized system could have significant positive impact on the practice of screening and prioritization of the full risk population.

Conclusions: Approaches that enable families to bridge the gap between initial warning signs of developmental delay and clinical diagnosis of autism quickly and effectively are critically needed for the field. Our tool demonstrates the feasibility of pre-clinical assessments and highlights the possibility of using mobile techniques to reduce bottlenecks and reach a larger percentage of the population in need.

111.006 Sex Differences in the Clinical Profiles of Children At Risk for Autism Based On the Modified Checklist for Autism in Toddlers (M-CHAT). N. N. Ludwig*¹, D. L. Robins¹ and D. A. Fein², (1)*Georgia State University*, (2)*University of Connecticut*

Background: The Positive Predictive Value (PPV) of the Modified Checklist for Autism in Toddlers (M-CHAT), has been shown to be higher for males than for females (Ludwig et al., *IMFAR 2011*). Given the long waitlists and high costs for ASD evaluations, there is a need to reduce the number of false positive females on the M-CHAT.

Objectives: The current study examined the sex specific clinical profiles of toddlers who received an ASD evaluation based on M-CHAT screen positive status in order to explore potential differences that may contribute to the differential PPV of the M-CHAT in boys and girls.

Methods: The sample included 218 males and 102 females (mean age=25.6 months, $SD=5.3$) who were evaluated based on screen positive status on the M-CHAT, a parent questionnaire administered at pediatric well-visits. Evaluations included autism diagnostic measures (ADOS, ADI-R, CARS), a developmental measure (Mullen Scales of Early Learning; Mullen), and parent report of history. Clinical judgment incorporated all data collected into a DSM-IV symptom count and final diagnosis. 156 toddlers were diagnosed with and ASD (121 males) and 164 toddlers were not (97 males). 72% of toddlers not diagnosed with ASD were diagnosed with another developmental delay.

Results: ANOVAs were conducted with sex and ASD status (ASD vs. non-ASD) as fixed factors and Mullen scores as dependent factors. Scores on the Fine Motor (FM) and Receptive Language (RL) scales were lower ($p's < .05$) in the ASD group compared to the non-ASD group. Scores on the Visual Reception (VR) and Expressive Language (EL) scales did not differ by sex in the non-ASD group; however, girls with ASD demonstrated lower ($p's < .05$) scores on these scales than boys with ASD. Scores on the Gross Motor (GM) scale were lower ($p < .05$) for girls than boys in the non-ASD group, and this effect was larger in the ASD group. ANOVAs were also conducted with sex and ASD status as fixed factors, and ASD symptom outcomes as dependent factors. Although there were no sex by ASD status interactions, there was a main effect ($p < .05$), of sex on the number of DSM-IV symptoms within the repetitive and restricted patterns of behavior domain (girls < boys).

Conclusions: This distinct pattern of findings suggests that there are differences in the clinical profiles of boys and girls considered at risk for ASD based on the M-CHAT. Generally, toddlers with ASD demonstrated lower scores on developmental outcomes than toddlers who were non-ASD. Girls with ASD demonstrated lower scores on the Mullen VR and EL scales than boys with ASD. Additionally, girls demonstrated lower Mullen GM scores and fewer DSM-IV symptoms within the repetitive restricted patterns of behavior domain than boys, despite ASD status. Future research will examine how these differences may be used in the development of

sex-specific scoring algorithms to increase the PPV of the M-CHAT.

111.007 Abnormalities of the Serotonin-NAS-Melatonin Pathway in Autism Spectrum Disorders. C. Pagan^{*1}, H. Goubran Botros¹, G. Huguet¹, M. Leboyer², R. Delorme³, J. M. Launay⁴ and T. Bourgeron⁵, (1)*Institut Pasteur*, (2)*INSERM U 955, Hôpital Chenevier-Mondor*, (3)*Hôpital Robert Debré*, (4)*Hôpital Lariboisière*, (5)*Paris Diderot University*

Background:

Autism spectrum disorders (ASD) are a heterogeneous group of severe developmental disorders. In more than half of the patients, major sleep problems are present and dramatically affect the quality of life of the patients and their family. The sleep problems are thought to be heterogeneous and not specific to ASD, but they should not be neglected. Indeed, they may constitute one of the first features detected in babies at risk for ASD. In addition, the quantity and quality of sleep could be ameliorated by appropriate behavior therapies and/or pharmacological treatments. One of the molecules that regulate the sleep-wake cycle is melatonin. This molecule is synthesized through serotonin during the dark phase of the day and is important for the circadian entrainment of the clock.

Objectives:

We previously showed that melatonin synthesis was reduced in patients with ASD. Here, we explored all components of the serotonin-NAS-melatonin pathway in a large cohort of patients with ASD, their parents and controls.

Methods:

Serotonin, melatonin, the intermediate metabolite N-acetylserotonin (NAS), and the two enzymes AANAT and ASMT was assessed in the blood (whole blood, plasma, or platelets according to the parameters considered) of more than 193 patients with ASD, their first-degree relatives (at least 226 parents and 60 unaffected sibs) and a group of more than 222 controls.

Results:

As previously described, patients with ASD displayed elevated blood serotonin. Taking as a threshold the 90th percentile of the control group (680 nM), hyperserotonemia was observed in 47% of patients with ASD. Serotonin was not found to be significantly elevated in their first-degree relatives. In contrast, plasma melatonin was significantly decreased in patients with ASD and their relatives compared to controls. Taking as a threshold the 10th percentile of the control group (0.09 nM), melatonin deficit was observed in 63% of patients with ASD, 35% of their parents and 31% of sibs. The melatonin decrease was associated with significantly reduced activities of both enzymes involved in melatonin synthesis, AANAT and ASMT, measured in blood platelets. Melatonin level was significantly correlated with ASMT activity in all status groups, and the strongest correlation was observed for patients with ASD (n=201, linear regression: $r^2=0.57$, $p<0.0001$). Finally, the intermediate metabolite NAS was significantly elevated in patients with ASD and in their relatives compared to the control group. Taking as a threshold the 90th percentile of the control group (37.3 nmol/109 platelets), NAS was elevated in 60% of patients, 29% of parents and 35% of unaffected sibs. Based on questioners, we showed that abnormal serotonin-NAS-melatonin pathway was significantly associated with the presence of sleep disorders.

Conclusions:

Low melatonin and increased NAS represent relevant biomarkers for a subset of patients with ASD. These data also indicate that melatonin deficit and accumulation of NAS results from a reduction of ASMT activity. These abnormalities have a complex inheritance and/or a non-inherited component, but the high frequency of melatonin deficit observed in parents suggests that this deficit may be a risk factor of having a child with ASD.

111.008 Behavioral Markers Predictive of ASD in High-Risk Infants At 6 Months. J. A. Brian^{*1}, L. Zwaigenbaum², S. E. Bryson³, W. Roberts⁴, I. M. Smith³, P. Szatmari⁵, C. Roncadin⁶, N. Garon⁷ and T. Vaillancourt⁸, (1)*Holland Bloorview/ Sick Kids*, (2)*University of Alberta*, (3)*Dalhousie/IWK Health Centre*, (4)*University of Toronto*, (5)*Offord Centre for Child Studies & McMaster University*, (6)*Peel Children's Centre*, (7)*Mount Allison University*, (8)*University of Ottawa*

Background: Prospective studies of high-risk infants provide the opportunity to characterize the earliest signs of ASD using direct observational data. While robust behavioral markers of ASD have been identified at 12 months and later, there is still uncertainty about whether earlier markers can be detected.

Objectives: To identify behavioral markers at 6 months predictive of ASD at age 3 years, using longitudinal data from a high-risk cohort of younger siblings of children with ASD.

Methods: Participants included 231 high-risk infants (HR; younger siblings of children with ASD) and 145 low-risk comparison infants (LR) followed from age 6 months to 3 years. Early markers of ASD were assessed using the Autism Observation Scale for Infants (AOSI; for details see Bryson et al, 2008) at 6 months. Clinical best estimate ASD diagnoses were determined using the ADI-R, ADOS and DSM-IV-TR blind to prior assessments. AOSI item scores were compared in HR infants diagnosed with ASD at 3 years (HR-ASD), HR infants not diagnosed with ASD (HR-N) and LR infants, with further pair-wise comparisons among these groups. To take into account multiple comparisons (as well as intercorrelations among AOSI items), critical p-value for significance was set at $p<.01$.

Results: Of 231 high-risk infants, 51 were diagnosed with ASD at 3 years (22.1%). HR infants (both HR-ASD and HR-N) differed from LR infants with respect to reduced or atypical anticipatory social responses, eye contact, and social referencing. Only reduced/atypical motor control was ASD-specific at 6 months; that is, more common in HR risk infants who developed ASD compared to both HR-N and LR infants. In addition, HR-ASD differed from LR infants on reactivity and engagement of attention (see Table for details).

Conclusions: Based on behaviors observed on the AOSI, HR infants (regardless of ASD outcome) differed from LR infants at 6 months in respect to reduced/atypical anticipatory social responses, eye contact, and social referencing. Only reduced/atypical motor control distinguished ASD within the HR group at 6 months; i.e., was more common in HR infants who developed ASD compared to both non-diagnosed HR infants, as

well as LR infants. In addition, HR infants with ASD differed from LR infants at 6 months on observed reactivity and engagement of attention, consistent with parent-reported temperamental profiles (Garon et al., 2008; in preparation). These findings will be discussed in the context of the evolving behavioral profile observed at subsequent time points, and in relation to current hypotheses regarding the role of attention and affect regulation in the early expression of ASD vulnerability.

Core Deficits Program

112 Language Development

This session provides a review of language development in children with ASD. Papers address topics including the rate of nonverbal children with ASD, atypical syntax and narrative skills, and changes in language across development.

112.001 Longitudinal Look At Expressive, Receptive and Total Language Development in Individuals with Autism Spectrum Disorders. A. Cariello^{*1}, S. E. Tolley², M. D. Prigge¹, E. S. Neeley², N. Lange³, A. L. Alexander⁴, A. L. Froehlich¹, E. D. Bigler¹ and J. E. Lainhart¹, (1)University of Utah, (2)Brigham Young University, (3)McLean Hospital, (4)University of Wisconsin

Background: Individuals with autism spectrum disorders are currently classified with impairments in both expressive and receptive language. Language impairments range from difficulty acquiring spoken language and in pragmatic language to never acquiring language. Longitudinal investigation of the development of specific types of language is needed from childhood into late stages of adulthood for individuals with autism. Doing so will help understand specific developmental trajectories and targets for new language interventions.

Objectives: Our goal was to understand longitudinal development of receptive, expressive, and total language in autism and controls by examining repeated measures of the CELF language assessment instrument.

Methods: Participants included 71 male controls (age range 3-39yrs at first test) and 106 males with autism (age range 3-45yrs at first test). Expressive, Receptive and Total language function was obtained from the Clinical Evaluation of Language Fundamentals (CELF) administered 1 to 4 times over 13 years (for a total of 324 assessments). A diagnosis of autism was obtained

using the Autism Diagnostic Interview (ADI) and the Autism Diagnostic Observation Schedule (ADOS). In order to compare across multiple versions of the CELF (Preschool, CELF-3, CELF-4) we created z-scores for each test version based on the control sample. Linear Mixed models examined linear and nonlinear age effects as well as group by age interactions.

Results: The z-scores for receptive, expressive and total language were significantly lower in the autism group than controls (all $p < .001$). For receptive language the autism group showed age related increase in z-score (on average 10% per year), which differed significantly from controls (on average 1.56% per year; group by linear age interaction ($p < .001$) with a trend toward group difference in nonlinear age related changes ($p = .097$). For expressive language we did not find age related changes in autism. For total language the autism group showed linear age related changes ($p < .001$) that did not differ significantly from controls.

Conclusions: As expected the expressive, receptive and total language z-scores are decreased in high functioning individuals with autism compared to typical development. Receptive language performance in the autism sample increased over time, which was different than in typical development. However, this trend in improved CELF performance was not found in expressive language. Age related changes in total language were drive by receptive z-scores. To our knowledge, this is the first longitudinal study looking at raw age-related changes of language in autism. This may show continued increase in receptive language ability in individuals with autism and the need to create interventions that improve expressive language function.

112.002 Language Development in Children with ASD: A Longitudinal Study of Grammar and Lexicon. E. C. Kelty*, D. A. Fein and L. Naigles, *University of Connecticut*

Background: Within language development research, there is an ongoing debate about the relationship between lexicon and grammar acquisition. While lexical items must be learned, grammatical rules may be part of a domain-specific system (Pinker, 1999) or may be learned through domain-general mechanisms as a continuation of lexical learning (Bates & Goodman, 1999). Children with autism spectrum

disorders (ASD) provide a unique perspective: research findings are mixed as to whether children with ASD have intact grammar (Tager-Flusberg, 1994) or show impairments (Eigsti et al. 2007). Could children with ASD show a dissociation of these areas of development? If so, are lexicon and grammar simply delayed or do they have deviant trajectories? We address this using a longitudinal data set and growth curve analyses (Singer & Willett, 2003).

Objectives: We will explore the trajectories of lexical and grammatical development in young children with ASD and typically-developing (TD) children.

Methods: The current study followed 28 children with ASD and 30 TD children, assessing their language comprehension and production at six visits spaced four months apart, and again at an outcome visit two years after visit 6. The groups were matched on language ability at the first visit (at visit 1, TD children: Mental Age = 20 months, mean CDI = 118; children with ASD: Mental Age = 33 months, mean CDI = 94). Through parent-child play sessions, we assessed lexical development (type-token ratio; TTR) and grammatical development (mean length of utterance; MLU).

Results: We analyzed children's TTR for nouns and verbs, in order to explore lexical development with a production measure, and found significant group differences: whereas the TD children's noun TTR increased as they learned more types, their verb TTR decreased, suggesting that they are using the verbs they do know more flexibly. In contrast, the children with ASD showed increases in both their noun and verb TTRs, suggesting that they were not increasing their verb flexibility and instead used different types over many situations. However, MLU (tapping grammatical development) showed significantly different slopes across the groups, with the ASD group progressing more slowly over time than the TD group. At the outcome visit, children with ASD do score significantly lower than TD children on both lexical and grammatical measures (Test of Auditory Comprehension of Language vocabulary: $t(28)=7.05, p<.01$; TACL syntax: $t(28)=8.55, p<.01$).

Conclusions: These results illustrate an interesting pattern: while TD children show a characteristic pattern of increase in their MLU, TTR is more complicated and dependent on whether we look at noun or verb development. Children with ASD show continual improvement in some lexical aspects (nouns) but delayed grammatical development. This may point to a dissociation in the lexical and grammatical development of children with ASD, which bears on theories of language development overall.

112.003 How Many Children with Autism Spectrum Disorder Are Functionally Nonverbal?. P. Mirenda¹, I. M. Smith^{*2}, J. Volden³, P. Szatmari⁴, S. E. Bryson⁵, E. Fombonne⁶, W. Roberts⁷, T. Vaillancourt⁸, C. Waddell⁹, L. Zwaigenbaum³, S. Georgiades⁴, E. Duku⁴ and A. Thompson⁴, (1)University of British Columbia, (2)Dalhousie University / IWK Health Centre, (3)University of Alberta, (4)Offord Centre for Child Studies & McMaster University, (5)Dalhousie University/IWK Health Centre, (6)Montreal Children's Hospital, (7)University of Toronto, (8)University of Ottawa, (9)Simon Fraser University

Background: Historical estimates are that 50% of children with autism over the age of 6 are nonverbal (Lord & Rutter, 1994), meaning that they have few or no words or that they do not speak as their primary method of communication. However, in 2004, Lord, Risi, and Pickles provided data from the United States suggesting that approximately 14%-20% of children with autism remain nonverbal by age 9. These estimates may be biased, however, by the non-systematic sampling procedures.

Objectives: The purpose of this study was to estimate the proportion of children with ASD in Canada who remain nonverbal at the time of school entry, using a systematic sampling procedure and the same measurement criteria as Lord et al. (2004).

Methods: Data were drawn from the *Pathways in ASD* study and included 231 children from five Canadian provinces. At first assessment, within 4 months of diagnosis, the children's mean age was 40 months (range = 24-61 mo). The ADOS module and question 30 (overall level of language) on the ADI-R were used to define four language categories, as per Lord et al. (2004). These were: (a) fluent language; (b) phrases but not fluent (daily uses phrases ≥ 3 words which sometimes include a verb, and are comprehensible to others); (c) words but not 3-

word phrases; and (d) no consistent speech (i.e., "nonverbal," defined as fewer than 5 words total or speech not used daily). The proportions of children in each language category were calculated separately for ages 2-2:11, 3-3:11, and 4-4:11 at the time of diagnosis (T1) and at the time of school entry (T2, ages 6-7).

Results: Of the total sample at T1, 1.7% had fluent speech, 25.5% had phrases, 36.1% had words but no phrases, and 36.7% were nonverbal. At T2 (age 6-7), 54% had fluent speech, 24.2% had phrases, 12.1% had words but no phrases, and only 9.8% were nonverbal. A strong relationship was found between verbal level at T2 and age at T1. Of the 89 children diagnosed between ages 2-2:11, who were most comparable to those in the Lord et al. (2004) study, 20.1% remained nonverbal at ages 6-7 and 54.4% had fluent speech. Corresponding figures for 89 children diagnosed between ages 3-3:11 were 5.2% and 52.6%, and for 53 children diagnosed between ages 4-4:11 were 2% and 56%. All children in the nonverbal group, regardless of age of diagnosis, had cognitive age-equivalent scores \leq 21 months at T1 and scored \leq 29 months at T2.

Conclusions: In this sample, the proportion of Canadian children with ASD who were diagnosed at age 2 and who remained nonverbal after age 6 was similar to results reported by Lord et al. (2004). Overall, in our sample, approximately 10% of the children remained nonverbal by school entry. The children who remained nonverbal, regardless of the age of diagnosis, were those whose low mental ages at T1 remained relatively stable at T2.

112.004 Agreement Across Multiple Modes of Language Assessment in Minimally Verbal Children with Autism. C. Mucchetti^{*1}, K. Goods¹, K. K. Krueger¹, C. Kasari¹, A. P. Kaiser², J. P. Nietfeld², P. Mathy³ and R. Landa³, (1)University of California Los Angeles, (2)Vanderbilt University, (3)Kennedy Krieger Institute

Background:

Approximately 30-40% of children with autism remain minimally verbal past age 5, despite intense early intervention (Anderson et al., 2007). These children are underrepresented in research, thus there is little information about their abilities and development. This is partially due to difficulties inherent in assessing their skills,

such as behavioral challenges and spoken language limitations (Kasari et al., submitted).

Language is a primary concern with this population and is measured through direct assessment, observation and parent report. Current recommendations are that a combination of modes be used to assess language in minimally verbal children with autism (Kasari et al., submitted). However, little is known regarding relative accuracy and agreement across assessment modalities within this population.

Objectives:

This study evaluates agreement among multiple measures of language ability in minimally verbal children with autism. Parent report, direct assessment and observational measures were compared.

Methods:

Participants included 60 minimally verbal children with autism (M age = 6.32 years) from a multi-site social-communication intervention study. Mean developmental age was 4.01 years (Leiter-R age-equivalent). Participants had fewer than 20 words on a standardized language sample (M = 11.11). Data for this study was taken from the entry timepoint.

Parent report measures included Macarthur Bates Communication Inventory (MCDI; words produced, words understood scores) and Vineland Adaptive Behavior Scales (VABS; communication subscales). Direct assessments included Peabody Picture Vocabulary Test (PPVT; receptive vocabulary) and Test of Early Language Development (TELD; expressive, receptive subscales). Observational measures included a 20 min standardized language sample and data from the first two intervention sessions. Language sample and intervention session videos were transcribed and analyzed using the SALT protocol (Miller & Iglesias, 2008). The Number of Different Word Roots (NDWR) in each transcript was automatically calculated by SALT.

Results:

Partial correlations were calculated controlling for the effects of developmental age. Due to the number of correlations, p -values less than .01 were considered significant. Parent measures (MICDI, VABS) expressive scores were significantly correlated with NDWR from the language sample ($r=.56, p<.001$; $r=.34, p=.007$) and intervention sessions ($r=.45, p=.004$; $r=.45, p=.002$), but not TELD expressive scores ($r=.29, p=.07$; $r=.33, p=.02$). Observational data (NDWR from Language Sample, intervention sessions) were significantly correlated with TELD expressive scores ($r=.40, p=.002$; $r=.47, p<.001$). Receptive skills reported by parents (MICDI, VABS) were significantly correlated with PPVT scores ($r=.42, p=.008$; $r=.40, p=.005$) but not TELD scores ($r=.31, p=.06$; $r=.21, p=.16$). Assessments yielding age-equivalents were compared directly to each other. PPVT scores were significantly higher than VABS ($t=-3.12, p=.002$) and TELD ($t=7.27, p=.000$) receptive. TELD and VABS scores did not significantly differ for expressive ($t=.68, p=.50$) or receptive scores ($t=-1.13, p=.27$).

Conclusions:

Overall there was high agreement across assessment modalities for both receptive and expressive language. Parent report reflected expressive language observed in a naturalistic context and observations were significantly correlated with direct assessment. PPVT scores correlated with parent report, and yielded the highest estimate of participant abilities. TELD scores were not correlated with parent report of expressive or receptive language, indicating that this assessment may not reflect abilities observed by parents.

112.005 Detail and Gestalt Focus in Spontaneous Descriptions by Individuals with Optimal Outcomes From ASD. A. H. Fitch*, D. A. Fein and I. M. Eigsti, *University of Connecticut*

Background: Individuals with high-functioning autism (HFA) have consistently been found to focus on details, sometimes at the expense of the whole, or gestalt (Mottron et al., 2003; Happé & Frith, 2006). The tendency to focus on non-central details rather than the gestalt impacts story-telling (Barnes & Baron-Cohen, 2012), verbal memory (Hermelin & O'Connor, 1967), and other communication skills central to social interactions. Detail focus is of particular interest in our study of

individuals previously diagnosed with HFA, who no longer meet criteria -- who have achieved a so-called "optimal outcome" (OO).

Objectives: We aimed to identify differences in detail focus for individuals with HFA, OO, and typical development (TD), by evaluating the production, in spontaneous speech, of statements that included person-centered details and gestalt statements (likely to be frequent in the TD group data) as well as non-central details and unrelated statements (likely to be frequent in the HFA data). A central question was whether the OO group's speech would pattern more similarly to the TD or to the HFA group, because the degree of "detail focus" is non-diagnostic but quite prevalent in autism.

Methods: A total of 45 children and adolescents with HFA, OO and TD (15 per group) described a rich visual stimulus (a painting) for ten seconds, while tapping their index finger; there were six such trials. Responses were recorded and transcribed, and each utterance was coded for focus: person, non-central, extrapolation, gist, or nonsense/unrelated. To date, data from 27 participants has been coded (5 HFA, 8 OO, 14 TD).

Results: In this preliminary analysis of a small sample, results nevertheless clearly indicated that the HFA group produced significantly fewer gist statements than the OO group, $p = .008$; the contrast with TD approached significance, $p = .06$, with no difference between the OO and TD groups. There was a similar pattern for person-centered details: the HFA group produced significantly fewer than the TD group, $p = .002$; the contrast with OO approached significance, $p = .06$, and there was no difference between the OO and TD groups. We also found that both the HFA group and the OO group produced significantly fewer non-central details than the TD group, $p < .05$, contrary to our predictions.

Conclusions: Results suggest that OO individuals have largely "normalized" in the degree to which they focus on person-centered details and gestalts, such that they are indistinguishable from their TD peers. This is a particularly stringent test of detail/gestalt focus, because participants were describing pictures during a "dual-task" paradigm, which involves a significant cognitive load. These

results cannot distinguish between two possibilities: 1) individuals with OO had a more detail-oriented focus, which changed over development, or 2) their different early cognitive style was already less detail-focused, with the implication that this may related to their reduction in symptomatology.

112.006 Narrative Abilities and Internal State Language in Children with Autism Spectrum Disorder and Typically Developing Children. A. George*¹, M. R. Swanson¹, G. Serlin¹ and M. Siller², (1)*Hunter College*, (2)*Hunter College of the City University of New York*

Background: Narratives allow us to interpret, integrate, and organize socio-cultural information and personal experiences in meaningful ways.

Therefore, difficulty in formulating narratives limits access to this rich form of interaction and can affect social-emotional and communicative competence (Losh & Capps, 2003). Effective narrative telling depends on emotional and cognitive state interpretation. As autism spectrum disorder (ASD) is marked by a deficit in social-emotional, cognitive, and linguistic abilities, analysis of narrative practices provides a unique opportunity to examine the nature of these deficits. In prior research, children with ASD referred to internal states less often than typically developing (TD) children (Tager-Flusberg, 1995; Tager-Flusberg, 1992).

Objectives: The current study compares TD children and children with ASD using a storybook narrative retelling paradigm accompanied by standardized developmental, linguistic and cognitive assessments to examine differences in usage of cognitive and emotional terms as well as any relationship to performance on developmental measures.

Methods: The sample included 20 children with ASD ($M=86.25$ months, $SD=18.28$ months) and 23 TD children ($M=81.83$ months, $SD=19.62$ months) from ethnically diverse backgrounds. The Social Responsiveness Scale (Constantino, 2002) was used to rule out ASD in TD children and the Autism Diagnostic Observation Schedules-General (ADOS-G; Lord et al., 2000) to confirm diagnoses in children with ASD. The samples were well matched on chronological age, gender ratio (ASD, 17/3; TD, 19/4, M/F), and receptive language age (ASD $M=87.10$ months; TD $M=87.17$ months).

Participants were tested during a single laboratory visit at Hunter College, City University of New York. During the laboratory visit, children were shown a wordless illustrated book, either *Frog Goes to Dinner* (Mayer, 1974) or *Frog on His Own* (Mayer, 1973). Each story depicts situations in which characters express various emotional and mental states in response to actions of the protagonist. The child narrated the story to a researcher. Each session was audio and video recorded. Audio recordings were then transcribed and divided into utterances. Transcriptions were coded for narrative and linguistic variables by research assistants blind to group assignment. Building on prior research, we assessed structural and evaluative aspects of the narratives including story length, utterance count, verb and adjective count, and internal state language (Capps, et al., 2000; Tager-Flusberg, 1995). The two independent coders established strong inter-observer reliability for all measures (ICC = .78-.98).

Results: After controlling for the number of utterances, children in the ASD group used significantly fewer emotional words than the TD group, $t(41)=3.14$, $p<.01$. There were no group differences in usage of cognitive words, $p=.97$. The ASD group also produced significantly shorter and less complex narratives, using fewer words $t(41)=3.52$, $p<.01$, and fewer utterances $t(41)=3.61$, $p<.01$. The TD group used significantly more distinct verbs and adjectives, $t(41)=2.945$, $p<.01$ and $t(41)=3.08$, $p<.01$.

Conclusions: This research suggests that children with ASD produce significantly impoverished narratives when compared to TD children, specifically in the utilization of emotional language. However, we did not find significant group differences in cognitive language, suggesting that children with ASD may not display global deficits in use of internal state language.

112.007 A Comparison of Syntactic Skills in Children with Autism or SLI: Similar Performance, but Different Errors. N. Sukenik* and N. Friedmann, *Tel Aviv University*

Background: , Language impairment is common (although not universal) feature of autism-spectrum-disorder (ASD). It has been widely argued that language difficulties that affect some people with ASD can be understood as a subtype of specific-language-impairment (SLI). Past

studies have found that children with syntactic SLI show a very consistent pattern of impairment in language tasks assessing syntactically complex structures, including the comprehension and production of relative clauses, the repetition of syntactically complex sentences, and WH question production.

Objectives: , The objective of the current study was to see whether children with ASD would show the same error patterns as children with SLI. The tasks chosen for this research were the tasks that were the most sensitive to the syntactic impairment in SLI.

Methods: , Participants were 18 native Hebrew-speaking autistic children (16 boys) aged 8; 3 to 17; 6 years (mean = 11; 7, SD = 1; 8), who were rigorously diagnosed by a multi-disciplinary panel. Each child was administered six tasks: (1) picture description task involving the production of subject- and object-relative clauses; (2) production of Wh questions; (3) comprehension of relative clauses and *which*-questions in a sentence-picture matching task; (4) comprehension of relative clauses in a comprehension questions task; (5) repetition of syntactically complex sentences including object relatives, topicalized sentences, Wh questions, embedded sentences, structures with verb movement, compared with simple sentences, (6) verb inflection completion (subject-verb agreement and tense). These tasks were also administered to Hebrew-speaking children with syntactic-SLI. All comparisons between groups were conducted by applying the standard chi test and two-tailed T-test. We accepted $p < 0.05$ as the minimum acceptable level of significance.

Results: , The individual variation between ASD subjects was considerable. Although some of the participants with ASD showed significant difficulties in performing the syntactic tasks, the error patterns that were found in this group were markedly different from the known pattern of errors in previous studies of SLI. In the relative-clause and Wh questions production tasks, the children with ASD made errors that included many pragmatic and morphological errors, which do not occur in SSLI production. Furthermore, whereas SSLI children produce subject questions well, the ASD children struggled both in subject and in object questions. In the relative clause

comprehension task some ASD children did not show the asymmetry between subject- and object relatives, found for SSLI. In the repetition task, unlike children with SLI who had either errors that were lexical or grammatical, ASD children showed errors of perseveration, adding of information, answering a question instead of repeating it, substituting a target word with a word close to it semantically.

Conclusions: , This study challenges the view that language difficulties in ASD reflect comorbid SLI. Indeed, the errors of children with ASD did not look like those of any other population that we have studied in the past including children with intellectual disability or orally trained hearing impairment. The difficulties the participants with ASD showed on the syntactic tasks were of a completely different nature, which points to a different nature of the underlying deficit.

112.008 Does the Verbal Comprehension Index (VCI) Score of the WISC-IV:UK Detect Language Impairments in School-Aged Children with Autism Spectrum Conditions?. S. M. Staunton*¹, M. Murin², O. Baykaner², W. Mandy³, S. Anderson¹, J. Hellriegel⁴, C. Walters⁵ and D. H. Skuse¹, (1)*Institute of Child Health, UCL*, (2)*Great Ormond Street Hospital for Children NHS Foundation Trust*, (3)*Faculty of Brain Sciences, UCL*, (4)*University College London*, (5)*Cardiff University*

Background: Language impairment is a core feature of autism spectrum conditions (ASC). It can range from a difficulty understanding or using single words and short sentences to more subtle, higher level language difficulties. The Wechsler Intelligence Scale for Children® — Fourth Edition (WISC-IV^{UK}) is one of the most widely used cognitive assessments for school-aged children in the United Kingdom. Its Verbal Comprehension Index (VCI) evaluates particular aspects of linguistic ability, such as verbal concept formation and verbal reasoning. In clinical practice, general conclusions about the language development of children with ASC are often drawn from the VCI score. It is sometimes assumed that additional language testing is not indicated once a child's VCI falls within the average range.

Objectives: To examine the ability of the VCI score of WISC-IV^{UK} to detect receptive and expressive language impairments in a group of school-aged children with a diagnosed ASC.

Methods: A cognitive assessment (WISC-IV^{UK}) and language assessment (Clinical Evaluation of Language Fundamentals - Fourth Edition UK; CELF-4^{UK}) were individually administered to a sample of children (n=26) with a confirmed diagnosis of an ASC who were in their final year at mainstream primary school (Mean age: 11 years; 3 months). A comparison was made of the following composite scores for each participant: the Perceptual Reasoning Index (PRI) and Verbal Comprehension Index (VCI) of WISC-IV^{UK}; the Receptive Language Index (RLI), Expressive Language Index (ELI) and Language Memory Index (LMI) of CELF-4^{UK}.

Results: Just under two-thirds of the sample (17 children) performed within the language impairment range (mild, moderate or severe) on at least one of the three CELF-4^{UK} composites. However, 8 of these children (or 47% of those with language impairments) performed within the average range (score of 90 or above) on the VCI of WISC-IV^{UK}. The VCI did not detect linguistic difficulties in almost half of those scoring in the language impairment range on CELF[®]-4, therefore. Furthermore, the majority of children (7 out of 8 or 87.5%) in this undetected group had language difficulties in the moderate and/ or severe range (CELF-4^{UK}). The VCI proved accurate in detecting linguistic difficulties in children whose assessment profiles were characteristic of a Specific Language Impairment (SLI), however. Just over a quarter (26.9%) of the sample of 26 children had language profiles which met ICD-10 and DSM-IV criteria for SLI (with the exception of the coexistent ASC diagnosis) and the majority of their VCI scores (6 out of 7 or 85.7%) fell below the average range (i.e. 90 or below).

Conclusions: Undiagnosed language impairments are known to affect many aspects of the lives of children with ASC, including their psychological wellbeing, social interaction with peers, self-regulation of behaviour and ability to access the educational curriculum. Clinicians must be wary of drawing conclusions about a child's language development based solely on the VCI score, since it evaluates only certain aspects of linguistic development. Our findings highlight the importance of access to a comprehensive multidisciplinary assessment for

children with ASC, which includes a standardised language assessment.

Services Program

113 Young Children, Schools

113.001 1 Survey of Service Provision for Young Children with ASD Across Europe. E. Salomone*¹, H. McConachie², P. Warreyn³, J. Sinzig⁴, M. Noterdaeme⁵, L. Poustka⁶ and T. Charman⁷, (1)*Institute of Education, University of London*, (2)*Newcastle University*, (3)*Ghent University*, (4)*LVR-Klinik Bonn*, (5)*Klinik für Kinder- und Jugendpsychiatrie und Psychotherapie*, (6)*Central Institute of Mental Health*, (7)*Institute of Education*

Background: Worldwide, various treatment and educational approaches have been developed for children with ASD. However, little is known about the actual availability of such treatments across Europe. Additionally, there are no reports on the uptake of "complementary/alternative medicine" (CAM) approaches.

Objectives: To document the type and intensity of treatment and education provision, medications and the use of CAM in young children with ASD in Europe.

Methods: Parents of children with ASD aged 6 or younger were recruited through national parent organizations in 20 European countries and asked to complete a brief online survey (translated into 19 languages). The survey comprised questions on current provision of various treatment approaches, access to special education, use of medications and additional supports/aids and use of CAM. Data collection is ongoing and final results will be available by November 2012.

Results: Data collection yielded 1302 completed questionnaires so far. Based on initial screening regarding diagnosis and age of the child, approximately 80% of participants were considered eligible for the study. Speech and language therapy was the most frequently reported treatment currently received in most of the countries and overall 61% of parents reported receiving some speech therapy. Only in a minority of countries were the most frequently reported interventions behavioural interventions or parent training. The most frequently reported additional support was use of pictures exchange or use of visual aids (58%). Use of medication ranged from

< 10% to 40%. Preliminary analyses show only marginal use of CAM in this sample.

Conclusions: Preliminary results of this ongoing study identified huge variability across Europe in terms of type and amount of available treatments for young children with ASD. Current reception of both treatment and educational provision was found to be inconsistent with current recommendations in European national guidelines. These initial findings highlight the need to monitor treatment and education provision for children with ASD in Europe in order to contrast inequalities, specifically in relation to access to evidence-based interventions.

113.003 3 Challenges, Coping Strategies, and Unmet Needs of Families with a Child with Autism Spectrum Disorder in Goa, India. G. Divan¹, V. P. Vajaratkar^{*2}, M. U. Desai³, L. Strik-Lievers⁴ and V. Patel⁵, (1)*Sangath*, (2)*Sangath, Goa*, (3)*Yale University*, (4)*Università degli Studi di Milano*, (5)*London School of Hygiene and Tropical Medicine*

Background: Autism Spectrum Disorders (ASD) is being increasingly recognized in developing countries like India. There are a number of attempts to understand the experience of parenting a child with ASD, from around the world (Altiere et al, 2009, Gray, 2006, Luong et al, 2009, Shaked, 2005) However, little is known about the experiences of parents raising a child with ASD in the Indian context. With a population of over a billion, India has over 2 million children with ASD and the experience of parents can help inform policy as well as practice.

Objectives: This study aimed to describe the experiences of parents raising a child with ASD in the Western state of Goa, in India, with a view to understanding the challenges families face and their unmet needs during this parenting journey.

Methods: Twenty in-depth interviews and nine focus group discussions were carried out 98 participants, which included twelve parents of children with ASD and key community stakeholders such as special educators, teachers and parents of typically developing children. This qualitative data was triangulated to explore the experiences, life impact, and unmet needs of raising a child with ASD.

Results: Key findings suggest that raising a child with ASD puts a tremendous strain on families due to competing commitments, often leading to initial social withdrawal with later reintegration into social networks. Second, the impact is multidimensional, involving the personal sphere but also extending into the wider community with negative experiences of discrimination. Third, parents actively respond to these challenges through a range of approaches with help from existing and new social support networks and health care providers. Fourth, professionals from the health, education, and religious sectors have a low awareness of the unique needs of families living with ASD which leads to a considerable economic and emotional burden on families. Finally, as a consequence of these experiences, several unmet needs can be identified, notably for supporting increasingly isolated families and the limited access to multidisciplinary evidence-based services for ASD.

Conclusions: This qualitative study observed a range of adverse impacts associated with raising a child with ASD in Goa, India. Most parents undertook diverse strategies to address the challenges they faced, in the context of a health and social welfare system which had very limited awareness of, and services for, ASD.

113.004 4 Use of an Online Questionnaire to Explore Views of Educational Transition in the UK for Children with Autism Spectrum Disorder. S. Anderson^{*1}, M. Murin², S. M. Staunton³, J. Hellriegel⁴, W. Mandy⁵, O. Baykaner² and D. H. Skuse³, (1)*Great Ormond Street Hospital NHS Trust*, (2)*Great Ormond Street Hospital for Children NHS Foundation Trust*, (3)*Institute of Child Health, UCL*, (4)*University College London*, (5)*Faculty of Brain Sciences, UCL*

Background: In clinical practice, transition to secondary school is one of the most stressful events for children with autism spectrum disorder (ASD) and their families. Gaining an in-depth understanding of the factors which contribute to the heightened stress around this event would be immensely helpful for professionals supporting children and their families. It would allow clinicians to be more effective in their work and enable the provision of individualised, tailored transition planning and support.

Objectives: An online questionnaire was designed to ascertain the widest possible variety of views from a broad range of respondents.

Responses were obtained from young people with ASD, their families and professionals across the United Kingdom. We hoped that the inclusion a range of respondents would allow examination of opinions from different groups, thus mechanisms for support could be more clearly identified. We gathered demographic information and a range of qualitative information in response to specific questions about transition.

Methods: Links to the online questionnaire were circulated to all the main ASD support networks throughout the United Kingdom.

Results: Over a period of one year, over 400 responses were received. 70% came from parents or relatives of a young person with ASD. Children with ASD made up 4% of respondents and 17% were professionals interested in the area of transition, such as educationalists. The remainder of the respondents comprised adults with ASD and a category of 'other professionals' including researchers, family support practitioners and local charities. Preliminary analysis indicated children's main concerns were the size of the new school and navigation around it, bullying and concerns academic work would be too difficult. Parents expressed concern that children would struggle with organisation and orientation at secondary school with 74% of the parents indicated getting lost in the school was a worry, 78% worried about the school size. All teachers indicated that getting lost would be a worry (100%). Parents worried about children forming and sustain friendships (68%), difficulties misunderstanding social rules and being bullied, though a lower figure of 30% of parents indicated bullying as a worry. Children's mental health was a concern, with difficulties with anxiety, stress and depression being exacerbated by transition. The teachers' views mapped well with parental concerns for example both teachers and parents indicated travel to school as a worry (65%). Teachers also raised issues such as children with ASD being unable to identify sources of help when they experience difficulty at secondary school..

Conclusions: It is hoped that the findings from this study will contribute to both clinical and research understanding of the main stress factors for children with ASD and their families during transition. These findings may also be highly informative for education professionals supporting

children during transition and allow for tailored planning and intervention. A well-planned and supported transition could have a profoundly positive impact on mental health as well as a child's progression through secondary school. Our findings potentially can help reduce school refusal and the risk of placement breakdown for children with ASD at secondary level.

113.005 5 Expressed Emotion Among Indian Mothers and Fathers of Children with Autism: Cultural Variations in Parenting Approaches. R. S. Brezis*¹, T. S. Weisner¹, N. Singhal², M. Barua² and T. C. Daley³, (1)UCLA, (2)Action For Autism, (3)Westat

Background: Parents' degree of expressed emotion (EE) has been associated with psychiatric outcomes in a wide range of psychiatric disorders. Recently, EE also has been measured in parents of children and adults with autism (Benson et al., 2011; Baker et al., 2011), and shown to mediate increased behavior problems over time. At the same time, cross-cultural research has shown that EE varies widely across cultural contexts, and that Western parental expectations may not hold universally. For instance, a previous study of EE in India has shown that Indian parents of persons with schizophrenia have lower degrees of EE, which may lead to better outcomes (Wig et al., 1987). Finally, most cross-cultural and cross-diagnostic research on EE has focused on mothers' approach to their child, while relatively little is known about the self-perceived role of *fathers* in parenting their child. The present study presents the first cross-cultural examination of EE in Indian parents of children with autism, and also includes both mothers' and fathers' views of their child.

Objectives: The current study aims to establish: (a) whether Indian parents of a child with autism had lower rates of expressed emotion, as compared to US and European parents; (b) whether Indian mothers and fathers differ in their degrees of expressed emotion; and (c) whether Indian parents of children raise unique themes when discussing their children, that point to challenges and strategies that are less common in the West.

Methods: Mothers and fathers of 30 children with autism (aged 2-10) were interviewed as part of a larger study on the Parent-Child Training Program at Action for Autism, India, before they entered the training program. Parents were instructed to

speak for five uninterrupted minutes about their child with autism, and about their relationship with their child. The five-minute speech samples were recorded and translated from Hindi to English. The speech samples were coded according to standard Western criteria (Magana et al., 1986), for Warmth, Emotional Over-Involvement, Relationship, Critical and Positive comments. In addition, qualitative analysis of the speech samples identified and coded unique themes in what parents said.

Results: Preliminary analyses indicate that Indian parents of children with autism describe their children with a combination of criticism and positive comments, while their relationship with their child may be characterized as less warm using Western coding schemes. Using Indian thematic coding, and in the context of Indian family circumstances, however, these comments fit with training, respect, and family roles relevant in those contexts.

Conclusions: Examining the spontaneous descriptions of Indian mothers and fathers of children with autism using both standard EE coding, as well as culturally-relevant coding for the Indian family context, captures the meaning and relevance of EE more broadly than either alone. As awareness of autism expands globally, understanding the variety of parenting approaches to children with autism is crucial for developing culturally-appropriate treatments that take local environment and family context more fully into account. Future research will examine how parent support and training programs can incorporate contextual understanding and parent EE.

113.006 6 Understanding the Needs of Parents of Children with Autism Spectrum Disorders in India. A. Vaishampayan*¹ and E. I. Blanche², (1)*Therapy West Inc.*, (2)*University of Southern California*

Background: The family impact of bringing up a child with an autism spectrum disorder (ASD) is manifold. Common areas of concern identified in the Western literature are an increased demand on parents' time to coordinate the child's multiple services, reduced family participation in community activities, compromised personal time, increased financial hardship, reduced career flexibility, and increased stress over the child's future. This literature also reveals that parenting a child with special needs often results in life course

changes. While most of the research on the daily experiences of parents with autism was conducted in developed countries such as the United States, Sweden, Japan, and Australia, there is a need to understand the parents' experiences in other countries such as India.

Objectives:

- To understand the impact of parenting a child diagnosed with autism spectrum disorder in India.
- To identify the type of changes that parents made to their routines in order to accommodate their child's special needs
- To identify the supports that parents need in order to support bringing up their child with special needs.

Methods: Fifty four parents of children with ASD living in India answered an online survey made available through Qualtrics between April and October of 2010. The parents were recruited through an Indian parent support group. The survey comprised of 25 close and open ended questions. Besides demographic information, the questions pertained to the parents' experiences around the diagnosis of the child, the child's special services, the family's patterns of activities, and the family's support system. The responses were analyzed quantitatively using frequency distribution and qualitatively using thematic analysis. This poster focuses on data related to the impact of parenting a child with ASD, changes in family activities and the supports needed to bring up their child with special needs.

Results: Personal well being, socialization, family life and finances were the most frequently impacted areas with 93% of the parents stating that parenting a child with special needs had an impact on their lives and 70% of the parents reporting that a change in family activities occurred as a result of having a child diagnosed with ASD. Social activities such as vacations, short term outings such as dining out, or attending family functions were the most common activities reported as reduced or modified. Modifications commonly listed included the need for elaborate planning and parent turn taking. Parents expressed needs that were seldom met in

India. These included short term and long term respite care facilities, improved understanding from the community at large, better education facilities, and better trained service providers for their children.

Conclusions: While parents are the most important support system in the lives of all children, it is more so for children with autism spectrum disorders. It is therefore important to develop an in-depth understanding of factors that impact parenting children with ASD in all parts of the world. Research like this one contributes to the development of programs that target the parents' as well as the children's needs.

113.007 7 Effectiveness of the Early Intervention for Children with Autism Via Community-Based Health Check-Ups of Infants and Toddlers in Japan: A Preliminary Report From the Early Start Saga Model. T. Haramaki*¹ and T. Kuroki², (1)*Saga University*, (2)*National Hospital Organization Hizen Psychiatric Center*

Background: Since 2002, the government of Saga Prefecture, a state of Kyushu Island of Japan, has launched a unique screening system of young children with autism-spectrum disorders (ASD) in combination with community-based health check-ups of infants and toddlers. It consists of two steps of screening: the first step to check development of children and to serve an open consultation for their mothers regarding child rearing, and to screen any diseases and developmental abnormalities by pediatricians; the second step to detect children with high risk of ASD by well-trained public nurses. We previously reported the effectiveness of our screening system of community-based health check-ups by public health nurses for detecting young children with high risk of ASD (Haramaki et al., IMFAR 2012). Clearly, there is a strong need for the early intervention system for these identified very young high-risk children with ASD. In 2011, we started the subsequent programs, including the early diagnosis in collaboration with Hizen Psychiatric Center and the early intervention for ASD infants by employing the Early Start Denver Model (ESDM) as one of the main strategies and supporting for infant's mothers. One-to-one treatment sessions and counseling were provided for each child and mother, respectively.

Objectives: To examine the effectiveness of the Early Intervention System of Saga Model on

developmental progress of high-risk children with ASD as well as mental condition of their mothers.

Methods: All ASD high-risk children and their mothers were administered with the Saga Autism Early Intervention program. Developmental progress of children was measured by ADOS, PARS and other developmental scales. Depression and anxiety of mothers were assessed by self-report questionnaires.

Results: 20 children and mothers were recruited into the program since October, 2011. The data of all children showed remarkable progress on the developmental scale and a considerable decrease in ADOS scores. Concurrently, depression scale scores of mothers declined.

Conclusions: The one-to-one style of the early intervention strategies may be effective for treating children with ASD even at very young age of 18 to 36 months after birth. The ESDM appears very useful as the guideline for this life stage of ASD children. Supporting for young mothers also helps them to take daily care easier at home.

113.008 8 Being a Parent of a Child with Autism and/or Developmental Delay in Urban Ethiopia: Their Experience of Stigma, Perceived Autism Causes, Needs and Coping Strategies. D. Tilahun¹, B. Tekola*², A. Fekadu¹, Y. Baheretibeb¹, C. Hanlon¹ and R. A. Hoekstra², (1)*Addis Ababa University*, (2)*The Open University*

Background: Ethiopia is a low-income African country of 84 million people with limited health care facilities. The prevalence of autism in Ethiopia is unknown, but prevalence studies of general mental health problems and intellectual disabilities in other low-income countries suggest that these problems are at least as prevalent as in high-income countries [WHO, 2008]. There are only two trained child psychiatrists in Ethiopia and specialized child mental health clinics are limited to the capital Addis Ababa. The detection of, and appropriate care for, children with autism is further impeded by stigma and misconceptions of the causes of developmental disability and mental health problems. This project constitutes the first study of the experience of parents of a child with autism and/or developmental delay in Ethiopia.

Objectives: To examine 1) the level of stigma experienced by families with a child with

autism/developmental delay; 2) the explanatory models of parents about their child's condition; 3) what kinds of intervention parents have used and perceive are most needed; 4) the coping strategies used by the families.

Methods: Parents of consecutive attendees to the Yekatit 12 child psychiatric out-patient unit and the St Paul's clinic, Addis Ababa, who are diagnosed with autism and/or intellectual disability, are invited to take part. In a face-to-face structured interview, parents are asked questions on their social demographic background, their experience of stigma in the community (using an adapted version of the Family Interview Schedule), the perceived causes of their child's condition, the types of interventions they have tried and perceive are needed, and their coping mechanisms.

Results: Preliminary data collection and analyses suggest that parents with a child with autism/developmental delay experience some level of stigma in the community. All parents indicated they often need to explain to others that their child isn't like their picture of "crazy people", some parents experience embarrassment of their child's condition, but most parents do not try to hide their child's condition from others. Parents cited a mix of biological (e.g. meningitis infection or obstetric complications) and religious or supernatural factors as causes for their child's condition. Most families had tried both religious (e.g. attending the holy water, church or mosque) and medical treatment for their child. Some parents also beat or chained their child to attempt improving their difficulties. Parents expressed that adequate schooling and support for their child were most needed. Most families talked to family, friends and professionals, and engaged in prayer to cope with their child's difficulties.

Conclusions: This study highlights the stigma experienced by Ethiopian families living with a child with autism/developmental delay and their unmet needs. It is important to note that this study was conducted in parents of a child with a formal diagnosis, i.e. in families who had found their way to the clinic in the capital. The levels of stigma and unmet needs are likely to be higher in rural Ethiopia, and in families of children with similar problems who remain undiagnosed. A

larger data collection including families living in rural Ethiopia is planned.

113.009 9 Family Experience with Early Identification of Autism in a Low-Resource Community Based Setting. J. Odeh*¹, R. Harb¹, M. Jibril¹, J. Awad¹ and M. Elsabbagh², (1)*Palestinian Happy Child Centre*, (2)*McGill University*

Background: Early identification and intervention for children with autism is acknowledged to be a global priority, including in low- and middle-income countries (Khan et al., 2012). Anecdotal evidence suggests that there are substantial delays between the onset of parental concerns and subsequent diagnosis. Nevertheless, there is little known about parents' experiences of primary care in prior to diagnosis and their ability to access appropriate services.

Objectives: The current study was conducted to improve the knowledge base of primary care experience with parents of children with autism in a low-resource setting.

Methods: Semi-structured interviews were conducted with a group of parents of children diagnosed with autism recruited through the Palestinian Happy Child Center in the Palestinian territories. The interviews explored the timing and nature of early concerns, help-seeking, navigation of services, and the nature of support received from the community.

Results: The experience of families of children with autism prior to diagnosis was variable. Some parents reported no concerns about their children early on and emerging concerns over development, whereas others had concerns very early on. Nevertheless, most families experienced delays and complications in obtaining confirmation of a diagnosis and/or in understating the nature of the condition. Access to appropriate services was also a challenge for most parents, particularly financial barriers, fit with the child's needs, and variability in the extent to which services were evidence-based. Most parents receiving community-based intervention programs combining support for the child as well as the family reported that their child's progress often exceeded their expectations.

Conclusions: Our findings reinforce the need for supporting parents of children with autism who

play the primary role in improving their child's condition, especially in low-resource settings where specialized services are lacking.

113.010 10 Effectiveness of a Supported Screening in the Identification of Latino Children At Risk for ASDs. B. J. Anthony*¹, M. Biel¹, M. Minier², K. Linas¹, D. Jacobstein¹, I. Lorenzo-Hubert¹, S. Dos Santos¹ and R. Mendez¹, (1)*Georgetown University*, (2)*Unity Health Care, Inc*

Background: Screening in pediatric primary care is a key step in identifying young children with Autism Spectrum Disorders in order to expedite early behavioral and educational interventions that can improve outcomes. However, despite evidence that formal screening tools improve accuracy of identification over informal clinical assessment, the use of these tools to identify autism and other developmental delays 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. This presentation will present evidence for the effectiveness a *Supported Screening*—a multi-pronged intervention developed through a community participatory process including formative research with families and primary care providers (PCPs) and staff--to enhance identification of children at risk for ASDs seen in a large primary care center serving a primarily Latino population.

Objectives: The goals of *Supported Screening* 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: *Supported Screening* has been implemented at the Upper Cardozo site of Unity Health Care (UC-UHC) the largest provider of medical care in the District of Columbia and includes three main components: (1) outreach activities focusing on developmental milestones for families; (2) hands-on training for primary care providers (PCPs), involving 5 75-minute sessions covering a review of ASDs, screening with the adapted M-CHAT, interpretation and referral, engaging and activating families as well as addressing barriers identified in formative research; and (3) ongoing care coordination and support to families with a child identified at risk or

diagnosed with ASD or other developmental delays by family navigators with lived experience participated. 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: Pre-post training and follow-up evaluations showed significant increases in PCP knowledge of autism, the rationale and skills for evidence based screening and methods to increase disclosure of developmental concerns by families as well as positive changes in organizational climate attitudes toward screening process. The rate of M-CHATs completed for eligible children at 18 and 24 months has shown rapid growth, increased from less than 5% prior to the onset of Supported Screening to approximately 60% after 3 months of implementation to almost 100% 6 months into the intervention. No such changes were seen in other Unity Care sites. Referral completion following positive screens increased and satisfaction with family navigation services was high.

Conclusions: Universal screening for ASDs and developmental delays in primary care is facilitated by initial assessment of community/provider needs to inform outreach, family engagement, screening instruments and procedures and staff training. 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.

113.011 11 Using Research-Community Partnerships to Bridge the Science-Practice Gap in Children's Community Service Systems: Characterizing Studies and Collaborative Process. L. Brookman-Frazee*, *University of California, San Diego*

Background:

The growing field of implementation science is focused on increasing studies on improving methods to promote the systematic uptake of research findings and evidence-based practices into community-based service settings. A number of implementation research frameworks highlight the critical role of research-community partnerships to support the relevance and

organizational “fit” of interventions to maximize uptake and to build organizational infrastructures to support intervention sustainability. Further, policy directives from the National Institute of Mental Health, Centers for Disease Control and Prevention, and the Institute of Medicine call for improved collaboration between researchers and other community stakeholders to enhance the translation of research results into community-based care. Although there are growing numbers of research-community partnerships (RCPs) in the field of mental health services, particularly within pediatric service settings, more work is needed to explicate collaborative processes. The goal of the current study is to make more explicit much of the tacit knowledge that many researchers have gained through collaborative efforts.

Objectives:

The purpose of this study is systematically examine a representative group of RCPs that have been used to adapt evidence-based interventions, training, and broader implementation models to address mental health and behavioral issues for children including ASD, served in various community-based service systems. Specifically, a web-based survey completed by project principal investigators and community partners was employed to characterize the use of RCPs to tailor evidence-based intervention, training, and implementation models for delivery in across different childhood problems and service contexts.

Methods:

Through a comprehensive literature and grants search, independent review and consensus coding, 38 studies using RCPs for the purpose of developing, adapting or implementing an intervention in routine care services were identified. A web-based survey was administered to project principal investigators and community partners to characterize the projects and collaborative process. Survey items include both open and close-ended questions to identify common themes in study and RCP characteristics and processes.

Results:

Final mixed qualitative and quantitative data characterizing (1) characteristics of research studies using RCP models; (2) RCP functioning, processes, and products; (4) processes of tailoring EBPs for implementation in the community; and (3) investigator perceptions of the benefits and challenges of collaborating with community providers and consumers will be presented. Themes unique to ASD-specific studies will be highlighted.

Conclusions: Theme across many RCPs will inform future collaborative projects and the development of RCP theory. This presentation provides the larger context and larger framework for the other presentations in this symposium.

113.012 12 Proximal and Distal Outcomes From Use of Research-Community Partnerships to Adapt Evidence Based Practices for Community ASD Providers. A. Stahmer*, *Rady Children's Hospital, San Diego*

Background:

Increasing numbers of children with ASD are identified and represent a significant public health challenge. Although increasing numbers of intervention efficacy studies exist, dissemination of these interventions to community settings has been extremely limited. The use of participatory or collaborative models to develop effective interventions for the target service context is congruent with a recent call for a paradigm shift in how intervention research for the ASD population is conducted. Given the status of the evidence and community need for guidelines on how to work with children with ASD in community service settings, a collaborative approach among researchers and other ASD stakeholders is a promising method to ensure research-based practices are translated in a timely manner for these families.

Objectives:

Two projects will be discussed, each involving using a research-community partnership approach. The first utilized a consortium of community practitioners, funding agencies, researchers and families of children with ASD, working together to select an efficacious intervention to meet the needs of very young children (12-20 months) in early intervention

settings. The second involved a partnership between researchers and community mental health providers in which an evidence-based intervention protocol was developed for use in community mental health clinics serving youth with ASD (5 to 13 years). The purpose of this presentation is to (1) describe the use of RCPs to adapt evidence-based practices for use in community settings, (2) assess proximal outcomes and sustainability of the research-community partnership, and (3) discuss implications for translating evidence-based intervention for autism into the community.

Methods:

Descriptions of partnership development and outcomes are framed within a conceptual framework of research-community partnership based on literature from multiple disciplines on partnership, collaboration, and knowledge exchange. Outcomes including partnership synergy, goal attainment, and sustainability of the groups were obtained through surveys and study materials (e.g., meeting sign in sheets, published papers). All surveys were administered through a web-based instrument and analyses conducted in SPSS.

Results:

Results support proximal and initial distal outcomes of both the partnerships. Specifically, data indicate that the groups exhibited high levels of partnership synergy (i.e., adhered to the participatory research elements and had strong collaborative functioning). Both groups were highly productive as indicated by attainment of all initial goals and the large number of tangible products. Participants in both groups reported that the collaborative model provided a balance between research and community input in areas of goal development, scientific activities, and funding allocation. Data indicated strong participation and sustainability.

Conclusions:

Although demonstrating positive impacts of partnerships can be challenging, these projects provide initial empirical support for an RCP approach and support for measuring process

outcomes. Proximal outcomes and initial sustainability data support the potential for future positive distal outcomes. Data support the feasibility of developing and sustaining a highly synergistic and productive group who share common goals to improve community care through the implementation of EBPs. Implications for translating EBP into community settings serving individuals with ASD will be discussed.

113.013 13 Using Research-Community Partnerships to Facilitate Implementation of Effective Intervention in Classrooms Serving Students with Autism. D. S. Mandell*, *Perelman School of Medicine at the University of Pennsylvania*

Background:

Autism interventions that are proven efficacious in university-based research labs rarely are used in community practice and, when they are, often are not implemented with a high degree of fidelity and rarely achieve the same outcomes. We would argue that this discrepancy often results from the lack of research-community partnership in planning, implementation, and steps to ensure that the intervention sustains.

Objectives:

To present an innovative university-school district partnership designed to increase the use of evidence-based practice for students with autism in public schools, and to increase the sensitivity of and utility for these settings that are developed in research labs.

Methods:

The partnership began with two years of discussion regarding the needs of the district, potential research collaboration, and pilot evaluations. The initial focus of the partnership was on identifying and immediately addressing district needs regarding training and programming. District and research staff met regularly to discuss strategy and concerns.

Results:

These meetings and initial efforts led to a large-scale pragmatic trial in autism support classrooms, which in turn led to substantial policy and practice changes in the district. These

changes are supported by an ongoing contract between the district and the research team to provide consultation and support. This ongoing relationship has resulted in mutually beneficial natural laboratory to explore practical issues regarding the implementation of evidence-based practices, what interventions and training/consultation strategies work in this large, urban setting, and new models for thinking about implementation of evidence-based practices in public schools. Some important examples include changes in the intervention model to make it highly specified and simplified for classroom implementation, measurement and the development of strategies to address implementation climate and staff relationships in the classroom and school, and the emergence of tailored consultation strategies based on the skills and motivation of the classroom staff.

Conclusions:

This type of applied, community based research partnership requires considerable effort and trust to develop, but has important implications for public health approaches to changing community practice for students with autism.

113.014 14 A Glorious Mess: Implementing Evidence-Based Social Skills Interventions in Public School Settings. J. J. Locke^{*1}, M. Kretzmann², C. Kasari² and D. S. Mandell³, (1)*Perelman School of Medicine, University of Pennsylvania*, (2)*University of California Los Angeles*, (3)*Perelman School of Medicine at the University of Pennsylvania*

Background:

Children with ASD experience challenges in social reciprocity and communication that impede their ability to navigate social interactions, impacting the presence and quality of peer relationships. If left untreated, these social impairments exacerbate with age and continue through adulthood. Several interventions have been developed and tested to address this issue. Most recently, Kasari et al., (2012) conducted a randomized controlled school-based trial with 60 mainstreamed children with ASD from 56 classrooms in 30 schools. They found that peer-mediated interventions as facilitated by expert research personnel improved the social inclusion of children with ASD. However, at the 12-week follow-up, it was clear that the gains children with ASD made as a result of the intervention would

not sustain without additional support. These data showed that addressing social impairments within the school context can produce meaningful changes in children's social functioning, but also highlighted the challenges associated with schools' adopting and implementing social skills interventions to support children with ASD.

Objectives:

The purpose of this study was to conduct a randomized pilot a modified version of the Kasari et al. intervention with school personnel. The intervention was modified to provide schools with a cost-effective, feasible, and sustainable program to improve the social interactions of elementary-school-aged children with ASD with their peers.

Methods:

A total of 10 children with ASD, 10 school staff members, and 100 typically developing peers participated. School personnel and children with ASD were randomized in pairs to immediate treatment (IT) or a waitlist (WL) control. School personnel were provided with hands-on training with the target student and his/her peers during the lunch period that included didactics, modeling, and in vivo coaching on strategies to facilitate opportunities for children with ASD to engage in activities and/or play games with peers in the cafeteria and on the playground. For both groups, quantitative (e.g. social network centrality, measures of playground engagement with peers, fidelity of implementation) and qualitative (e.g. interventionist and observer field notes) data were collected at baseline, exit, a 6-week follow-up and each week of intervention.

Results: Analyses are ongoing. Mixed methods will be used to develop a complete understanding of implementation of the modified intervention for children with ASD in schools. Preliminary analyses will be conducted comparing the IT and WL groups on pretreatment scores of social network centrality and playground engagement. Qualitative data will be coded using the principles of grounded theory to examine factors related to implementation and quotes or themes will be used to support or refute results derived from quantitative data.

Conclusions: While the results suggest the effectiveness of this model, we encountered a number of barriers that interfered with the continued use of the intervention and were unable to address the issue of sustainability. We will discuss potential strategies to overcome child, classroom, and organizational barriers to implementing social skills interventions in school settings.

113.015 15 Evidence-Based Practice in Homeschools for Children with Autism Spectrum Disorders. C. A. Simmons*¹ and J. M. Campbell², (1)University of Georgia, (2)University of Kentucky

Background: Children with autism spectrum disorders (ASD) present with unique challenges within a traditional educational environment. Interactions between parents of children with ASD and education professionals are often marked by confusion, frustration, tension, and lack of cooperation that hinder the effectiveness of service delivery. Homeschooling children with ASD has increased in popularity and is considered a viable educational option by parents. Few empirical studies have focused on homeschooling children with ASD and none have investigated how educational experiences differ between homeschooled and non-homeschooled children with ASD.

Objectives: It is important to evaluate *why* parents make the decision to homeschool, and *what* educational experiences they are providing. The overarching goal of this exploratory research is to *discover* what educational experiences parents are providing in order to guide homeschooling decision-making and practice for students with ASD.

Methods: Focus groups were employed to glean preliminary information and revise a measurement instrument. Survey methodology is being employed to identify and describe: (a) parents' reasons for choosing to homeschool children with ASD, (b) challenges of educating a child with ASD at home, (c) amount and quality of evidence-based educational practices being delivered within the homeschool environment, (d) advantages and growth parents may experience through homeschooling, (e) impact homeschooling has on families' quality of life, (f) parent training and resources utilized, and (g) social and extracurricular opportunities for

homeschooled students with ASD. The questionnaire items comprise the domains of Demographic Variables, Satisfaction with Current Educational Programming, Ancillary Services Received, Extracurricular and Social Activities, and Bully Experiences that will be compared between homeschooling (n=50) and non-homeschooling groups (n=50). Data will be reduced within each domain to yield a total score. The overall inferential statistical analysis will utilize a multivariate analysis of variance (MANOVA) to evaluate if differences exist between groups. In the presence of a significant multivariate effect, we will utilize post-hoc univariate analysis of variance (ANOVA) to test for specific differences between groups. Descriptive analysis will be conducted to determine the amount and quality of evidence-based educational practices being delivered within the homeschool environment, to assess needs in the parents' current programming, and to document parents' experiences homeschooling.

Results: Data collection is in progress and will be collected with 100 participants (50 homeschool; 50 non-homeschool). Preliminary data indicate that parents of children with ASD who homeschool feel that schools could not adequately meet their child's needs and that the entirety of the programs they are providing are not guided by evidence-based practice for educating children with ASD.

Conclusions: The results of the current research study will hold significant relevance for improving the education of children with ASD, both in traditional schools and in homeschools. If parents of children with ASD are choosing to homeschool because of perceived weaknesses within the public education system, these findings might create a move to improve resources and training available. The results are expected to inform the development of a parent training program for parents who homeschool children with ASD to meet their identified needs.

113.016 16 The Relevance of "Realworld Evaluation" to Autism Intervention Research. T. C. Daley*¹, N. Singhal², M. Barua², T. S. Weisner³ and R. S. Brezis³, (1)Westat, (2)Action For Autism, (3)UCLA

Background:

In some settings, a researcher may encounter an autism intervention that has already been implemented within the community. This often occurs when an administrative unit has implemented or scaled up an intervention across a broad population of children (e.g., Nicholson et al, 2010; Anderson et al, 2006). It is also extremely common in low and middle income countries, where interventions for autism typically emerge from within the community rather than a research laboratory, and where randomized controlled trials and even quasi-experimental designs are not feasible. Interventions in these settings often involve a blended program, combining elements of tested programs and local models. For these situations in particular, there is value in examining the potential effectiveness of existing programs. Borrowing from the broader field of international evaluation, autism interventions can be examined through the lens of "RealWorld Evaluation" (RWE; Baumberger, Rugh & Mabry, 2006). This approach offers an opportunity to expand the knowledge base about available and effective interventions while working within the constraints typical of community settings.

Objectives:

The current study presents a systematic examination of a parent training model for autism following the RealWorld Evaluation approach.

Methods:

The first six steps of the RWE method were used to frame and conduct the evaluation, which was undertaken as part of a collaborative relationship between UCLA and an NGO in India called AFA. First, the program theory was used to develop a logic model for the program. Budget, time, data, and political constraints were examined and incorporated into the design. The evaluation took place over three consecutive sessions of a 12-week program. After extensive testing of measures to ensure appropriateness, a total of 48 parent dyads received pretest and posttest assessments using tools tied directly to the program theory. Assessing and addressing the strengths and weaknesses of the evaluation design has taken place in consultation with AFA.

Results:

Using the RWE approach, this evaluation demonstrated significant gains across multiple measures of parent knowledge, empowerment, acceptance, and skills. The use of a post-test comparison group further strengthened the validity of these findings. The greatest challenges to the evaluation were 1) large work loads required of the evaluation team, and 2) accommodating and accounting for naturally occurring variations in the intervention.

Conclusions:

The current study is the first use of the RWE approach for an autism intervention. Resulting in both formative and summative data, this study was successfully conducted with minimal changes to the existing structure, content and procedures of the program. RWE was developed for those working under budget, time, data and political constraints. As we seek to understand more about effective and culturally appropriate intervention approaches for children in diverse contexts, a RWE process has particular salience, particularly where there is little infrastructure and limited expertise, or simply no real possibility at present to support more rigorous research designs.

113.017 17 Effects of an Implementation Science Approach to Professional Development for Children and Youth with ASD. S. Odom*¹, A. W. Cox² and M. Brock³, (1)*University of North Carolina*, (2)*Frank Porter Graham Institute, University of North Carolina - Chapel Hill*, (3)*Vanderbilt University*

Background: Operating from an evidence-based practice and implementation science perspective, the National Professional Development Center on Autism Spectrum Disorders (NPDC) in the United States has as its goal to promote the use of evidence-based practice in programs for students with ASD. This center model has been implemented in 12 states.

Objectives: The objectives of this presentation will be to describe the evaluation of the NPDC system as it relates to teachers' use of EBPs in their classrooms, the changes in program quality, students' accomplishment of goals, and adoption of the NPDC model in states.

Methods: In this evaluation, the NPDC model was initially implemented at multiple public schools in 12 states in the United States. Teachers and

state technical assistance teams completed an online course and then participate in multiday intensive training with NPCD staff. Ongoing coaching was provided after the training. In this evaluation design, the Autism Program Environmental Rating Scale (APERS), a 61 items assessment measure, was administered at the beginning of the implementation year in a school and again at the end. At the beginning of the year, teachers and research staff created goal attainment scales (GAS) for prioritized learner goals. The GAS is a behaviorally anchored rating scale that rates student progress toward prioritized goals on a five point continuum. Teachers also reported the EPBs they used in their classes at the beginning of the year and the end of the year. Also, research staff collected fidelity data on teachers' use of specific EPBs in their classrooms using a fidelity checklist established individually for different practices. In addition, at the end of the work with the state programs, research staff collected information on the number of initially identified sites implementing the NPDC model, and the number of additional sites implementing the model that state personnel established independent of NPDC staff.

Results: Across the year, all subdomains and the total APERS scores increased significantly from fall to spring observations. The mean effect size was $d = 1.10$ and $d = 1.28$ for preschool elementary and middle school/high school sites, respectively. Teachers reported using significantly more EPBs in their classrooms, with a pre-post effect size of $d = 1.35$. Teacher fidelity of implementation increase across the year with patterns of "fast" (for 84% of the EPBs used) and "slow" (for 16% of the EPBs used) progresses toward the criterion level of implementing with 80% fidelity. Ninety-eight percent of the children made progress on their goals, with 78% of the targeted goals meeting or exceeding criteria. At the end of the evaluation, NPDC staff and state personnel had administered the NPDC model in 58 schools, and the states had expanded the model to an additional 110 schools.

Conclusions: The NPDC model was associated with improvements in program quality, increased teacher use of EPBs, and increases in student goals. The evidence for efficacy, while suggested, will require testing the model using a randomized control study, which is now being planning process.

113.018 18 Updated Review of Evidence-Based Practices for Children and Youth with Autism Spectrum Disorders. C. Wong¹ and S. Odom^{*2}, (1)University of North Carolina at Chapel Hill, (2)University of North Carolina

Background:

Evidence-based intervention practices (EBPs) for children with ASD are the basis on which effective programs are built. In their previous review and analysis of the literature from 1997-2007, the National Professional Development Center on ASD (NPDC) identified 24 practices that met the evidentiary criteria they had established. The research on focused intervention practices has accelerated in recent years, requiring an ongoing process for updating and communicating the most current scientific knowledge about practices to practitioners and families.

Objectives:

The purpose of this poster session is to describe the process that NPDC followed in identifying EBPs for children and youth with ASD and the results of the updates reviews of the literature.

Methods:

Using five databases (EBSCO, EMBASE, Medline, ISI, Sociological Abstracts) and a range of descriptors (e.g., autism, Asperger, intervention), the initial search generated 23,000 articles published between 1990 and 2011. After screening to ensure articles employed an experimental, quasi-experimental or single case design that tested and intervention with children and youth having ASD, the number of articles was reduced to 1,085. Criteria for determining methodological acceptability of individual were developed. One hundred forty reviewers completed training, met inter-rater agreement criteria, and evaluated the acceptability of the article methodology. Articles identified as acceptable were sorted using categories for practices established by the previous NPDC review and the National Standards Project. A final determination was then made about whether a practice meets the level of evidence necessary to be classified as an EBP using the following criteria: (a) two high quality experimental or quasi-experimental design studies, or (b) five single case design studies conducted by three

different research groups and involving a total of 20 participants across studies, or (c) there is combination of research designs, which must include at least one high quality experimental/quasi-experimental design and three high quality single case designs.

Results:

To date, reviewers have completed evaluations of 935 reviewed articles (86%) with the rest of the review being completed in the next month. Five hundred eleven articles (59 group design studies, 452 single case design studies) have been accepted as providing scientific evidence. Content analyses of procedures produced 31 different practices that appear in the table below.

Conclusions:

The focused intervention literature for children with ASD has been activity and high quality. The revised literature search and analysis by staff of the NPDC has identified practices that will provide a solid, empirical basis on which to design programs for children with ASD.

Table 1. Evidence-based Practices

| | | | |
|--|-----------------------------------|---------------------------------------|---------------------------|
| Antecedent-based interventions | Functional behavior assessment | Picture exchange communication system | Social skills groups |
| Cognitive behavioral intervention | Functional communication training | Pivotal response training | Speech generating devices |
| Computer-aided instruction | Imitation-based interaction | Prompting | Structured work systems |
| Developmental relationship-based treatment | Massage/touch therapy | Reinforcement | Task analysis |
| Differential reinforcement | Modeling | Response interruption/redirection | Time delay |

| | | | |
|-------------------------|--|-------------------|-----------------|
| Discrete trial teaching | Naturalistic intervention | Scripting | Video modeling |
| Exercise | Parent-implemented intervention | Self-management | Visual supports |
| Extinction | Peer-mediated instruction and intervention | Social narratives | |

113.019 19 Ameliorating Family Impacts Among Children with ASD: The Role of Health Care Quality. K. E. Zuckerman*, O. Lindly and C. Bethell, *Oregon Health & Science University*

Background: Children with Autism Spectrum Disorder (ASD) have complex health and social needs, and as a result, families of children with ASD experience deleterious employment and financial impacts. Quality health care, minimally including adequate health insurance coverage and receipt of medical home care, may mitigate employment and financial impacts on families.

Objectives: To examine family employment and financial impacts experienced among children with special health care needs with ASD (CSHCN+ASD) compared to CSHCN without ASD (CSHCN-ASD), in addition to the potentially mediating influence of quality health care on family impacts among CSHCN+ASD.

Methods: Nationally representative data weighted to represent the non-institutionalized population of U.S. CSHCN age 3 to 17 years were gathered from the 2009/10 National Survey of Children with Special Health Care Needs. Weighted logistic regression, controlling for socio-demographic differences, was used to examine financial and employment problems in 3025 CSHCN+ASD compared to 33 948 CSHCN-ASD. Employment and financial impacts were defined, respectively, as: CSHCN whose health conditions caused family members to cut back or stop working and CSHCN whose health conditions caused the family financial problems. Quality health care, conservatively defined as the receipt of care within a medical home and health insurance adequacy, was entered into the regression model as an independent variable to observe its effects on family financial and employment outcomes among CSHCN+ASD.

Results: Compared to CSHCN-ASD, CSHCN+ASD had higher adjusted odds of having a family member who cut back or stopped working due to their child's condition(s) (20.6% versus 57.1%; AOR: 5.32, 95% CI: 4.61-6.13) and having a family that experienced financial problems due to their child's health care needs (19.3% versus 43.2%; AOR: 3.36; 95% CI: 2.90-3.89). When CSHCN+ASD had quality health care, employment and financial impacts were lessened: Compared to CSHCN+ASD with inadequate health insurance, CSHCN+ASD with adequate health insurance had lower adjusted odds of having a family member who cut back or stopped working due to the child's condition (64.0% versus 50.6%, AOR: 0.60, 95% CI: 0.45-0.80) or who experienced financial problems (58.5% versus 29.2%, AOR: 0.31, 95% CI: 0.23-0.42). Similarly, relative to CSHCN+ASD who did not receive medical home care, CSHCN+ASD who received comprehensive, coordinated care within a medical home were less likely to experience family employment impacts due to their child's condition (60.1% versus 45.4%, AOR: 0.64, 95% CI: 0.48-0.86) and financial problems (48.1% versus 26.0%, AOR: 0.47, 95% CI: 0.33-0.66).

Conclusions: Families of CSHCN+ASD experience higher rates of adverse financial and employment impacts than families of other CSHCN; however, receipt of quality health care may lessen these impacts. Systemic mechanisms promoting access to adequate health insurance and medical home care among CSHCN+ASD will be imperative to improving the family environments that shape the trajectories of this vulnerable population.

113.020 20 Knowledge Translation Strategies for Engaging Families in Biomarker Discovery. S. Prasanna*¹, A. A. Yusuf¹, E. Fombonne², L. Zwaigenbaum³, S. W. Scherer⁴ and M. Elsabbagh¹, (1)McGill University, (2)Montreal Children's Hospital, (3)University of Alberta, (4)University of Toronto

Background: Miscommunication regarding the promise of biomarker discovery for supporting earlier identification and diagnosis of autism has led to controversies and unnecessary hype surrounding the true value of this research (Walsh et al., 2011). Our aim was to develop strategies to clarify the state of the science in biomarker research for families affected by autism and to obtain feedback regarding the realistic impact such biomarkers can have on early diagnosis and intervention in ASD. Specifically, we used

knowledge translation (KT) strategies to explore current beliefs and awareness among families about early identification and intervention in ASD and its relation to the biomarkers discovery agenda. KT is defined as the exchange, synthesis and ethically-sound application of knowledge within complex systems of interactions among researchers and knowledge users (Canadian Institutes for Health Research).

Objectives: 1) to examine families' knowledge (including misconceptions), attitudes and expectations towards ASD biomarker research in early identification and intervention, 2) to resolve misconceptions surrounding the current state of science, and 3) to gain feedback from families as to how such biomarker could improve their lived experience.

Methods: Participants in this project were one biological parent from each of the families involved in large-scale national studies. An extensive literature review was conducted to guide the design of an interactive survey. Survey questions elicited information in the following domains – 1) socio-demographics; 2) knowledge and attitudes about biomarker research; 3) expectations of the role of biomarkers; 4) preference and utility of knowledge of biomarkers in early identification and intervention of ASD. After survey completion, participants received feedback regarding their answers to questions related to their knowledge about biomarkers.

Results: Initial survey results provide insight into families' knowledge, attitudes and expectations about ASD biomarker research and its utility in early identification and intervention. Data obtained from the survey will be used to develop focus groups and interactive educational workshops to address misconceptions and to support families' understanding of the state of the science in biomarker research.

Conclusions: This project is a part of our ongoing research employing systematic research methodology in KT activities and to support the engagement of knowledge users in research. An Integrated Knowledge Translation (iKT) Toolbox is under development to support large-scale autism research studies to foster dialogue between researchers and key stakeholders including affected families.

113.021 21 A Pilot Program to Reduce Distress During Blood Draws in Children with Autism Spectrum Disorders. J. S. Russo* and C. A. Cowan, *Seattle Children's Hospital Autism Center*

Background: Blood draws for children with autism are very difficult. They can be so anxiety producing for the families of children with autism that they simply don't have them done for fear of what might happen. Many families have had prior experiences in the lab that they describe as negative, such as procedures requiring restraint or lasting for an extraordinary amount of time. The goal of this quality improvement project was to remove the barriers to children moving in and out of the lab quickly, and avoiding further negative associations with the lab.

Objectives:

- Eliminate wait times wherever possible
- Prepare the families
- Have staff present who are familiar with autism
- Have a coping plan for each kid coming to the clinic that day

Methods: After children were identified as needing a blood draw, each family was contacted by a Child Life Specialist to discuss prior lab experiences. A coping plan for that child was prepared and written down. The plans focused on distractors that would be helpful in the phlebotomy room. Families were scheduled to come to the lab, on a Saturday, at 30-minute intervals, to avoid waiting. Staff present on the day of the clinic included Autism Center staff (including at least one nurse), a Child Life Specialist, and a dedicated phlebotomist for the QI project lab. Families were met and escorted directly to the phlebotomy room. Phlebotomist confirmed identification with the family, and blood draw was performed. Cycle times were recorded and each family was contacted for a follow-up phone interview.

Results: Over the course of three different dates, 19 kids were scheduled in the pilot sessions. Time for the draws, from meeting at the door to leaving the phlebotomy room ranged from approximately 2 minutes to just over 6 minutes, excluding the family that took 29 minutes whose blood draw

was unsuccessful. Parental feedback noted significant satisfaction with cycle time, presence of staff familiar with autism, prior preparation including coping plans and materials on hand such as preferred video. Choosing a Saturday during less busy laboratory hours allowed both parents to attend or one parent could be home with siblings.

Conclusions: The three pilot sessions were a considerable success. These strategies demonstrate to parents and hospital staff that children affected by autism can successfully undergo painful procedures with minimal trauma and restraint. Preparation of staff and families are key components, which can be replicated in other settings such as immunization clinics, radiology procedures, emergency room visits and surgical/medical hospitalizations.

:

113.022 22 Screening for Autism Spectrum Disorders in Medical Checkups At 36 Months Can Predict Later Adaptive Functioning in Nursery School. M. Tsujii*¹, H. Ito², F. Someki², S. Nakajima², N. Mochizuki², N. Takayanagi² and W. Noda², (1)*Chukyo University*, (2)*Hamamatsu University School of Medicine*

Background: Early detection and intervention for autism spectrum disorders (ASD) is important because it may lead to better long-term outcomes. In Japan, local governments are legally obliged to conduct a medical checkup for all children whenever they reach the ages of 18 and 36 months. This checkup system is suitable for the detection of ASD because all children receive a checkup regardless of their parents' knowledge of developmental disorders or socioeconomic status. Nevertheless, the current form of checkups focuses on physical and intellectual development, and most local governments have not yet introduced systematic screening for ASD.

Objectives: We collaborated with a local healthcare center and introduced a systematic screening system for ASD in the medical checkup for 36-month-olds. To assess the validity of the system, we examined whether the screening results could predict later adaptive functioning in nursery school.

Methods: The Pervasive Developmental Disorders Autism Society Japan Rating Scale (PARS) was

used for screening. The PARS is an interview-based assessment tool, and it has been previously validated in terms of its ability to discriminate between individuals with ASD and normal controls and in terms of its satisfactory correlation with the Autism Diagnostic Interview-Revised (ADI-R) (Ito et al., 2012). We used the 12-item short form of PARS (Adachi et al., 2008). Health nurses at the local center were trained in using the PARS through lectures from clinical psychologists specialized in developmental disorders. In the first year of the trial, the psychologists and nurses concurrently conducted the PARS, and discrepancies in scoring were resolved through lectures. From the second year, health nurses individually conducted the PARS. The present study used data from the second year. One year later, the children's adaptive functioning in nursery school was rated by their nursery teachers, using the Nursery Teacher's Rating Developmental Scale for Children (NDSC). We obtained complete data from 287 children (150 boys). The study protocol was approved by the institutional review board of the Hamamatsu University School of Medicine, and it complies with the guiding policies and principles for experimental procedures endorsed by the National Institutes of Health. There is no conflict of interest.

Results: The PARS score correlated with scores on the NDSC subscales, especially the Communication ($r = -.53$), Sociality ($r = -.39$), Attention ($r = -.40$), Self-care ($r = -.39$), and Gross Motor ($r = -.36$) subscales. Children who had scored above the cut-off on the PARS were found to have a high risk (40.9–59.1%) of low adaptive functioning (below the 10th percentile) as per these NDSC subscales. Relative risk ranged from 10.19 to 11.18.

Conclusions: We found that screening for ASD in a medical checkup at 36 months, which is conducted by a health nurse, can effectively predict later adaptive functioning in nursery school.

113.023 23 Challenges and Perceptions of Services Providers Working with Young Children with Autism Spectrum Disorder and Concurrent Problem Behaviors. M. Rivard* and D. Morin, *Université du Québec à Montréal*

Background: The presence of problem behaviors (PB) is a major challenge for intervention

addressing needs of young children with a diagnosis of autism spectrum disorder (ASD) or intellectual disability (ID). A previous study has shown that PB interferes with the improvement of social behavior following a program of early intensive behavioral intervention (EIBI; Rivard & al., submitted).

Objectives: 1) describe training, assessment and intervention tools currently used by staff involved in a public program of EIBI offered to children with an ASD and PB; 2) assess the needs for training, assessment and intervention tools, as perceived by staff of public rehabilitation centers.

Methods: Semi-structured interviews were conducted with 75 persons (first line staff, professional clinicians and managers) involved in a EIBI program across 8 public rehabilitation centers in the province of Quebec, Canada. The interview includes 25 questions about training, assessment and intervention tools.

Results: 90% of respondents said that they had worked during the past year with children who have PB. To the same extent, respondents mentioned that they need training on PB as well as training on early childhood. To assess PB, respondents use tests suitable for typically developing children or for adults with ID or ASD. The need for assessment tools addressing the specificities of children with ID or ASD has been mentioned almost unanimously. Children with PB receive the same services as other children with ID or ASD. The majority of respondents (88%), however, indicate that they have to adapt the program. Respondents identified many of the challenges they face when working with children with PB, their families and day care settings. Among others, the growing problem of access to resources has been highlighted.

Conclusions: The recent implementation of EIBI in rehabilitation centers in Quebec has brought many benefits for children with ASD. However, the programs put in place so far tend to privilege the development of preschool skills. Based on recent research findings about the efficacy of EIBI for children with PB, it is now important to return to key components of EIBI programs. The present study shows that staff perceived significant needs for training, assessment and intervention tools for PB. Subsequent phases of the research program

are therefore: 1) to validate a screening tool to detect and assess PB of children aged between 18 months and 6 years before their entrance in EIBI programs of our centers, 2) to conduct a study of prevalence and key factors associated with PB among children attending our rehabilitation centers, and 3) to provide a framework for intervention and supervision to improve services efficacy.

113.024 24 Family Relationships and Parental Stress in Only Child Versus Multiple Children Families in the Context of Autism Spectrum Disorders: A Pilot Study. L. Vismara*¹ and G. S. Doneddu², (1)University of Cagliari, (2)Centro Disturbi Pervasivi dello Sviluppo Azienda Ospedaliera Brotzu

Background: Parenting stresses have consistently been found to be higher in parents of children with autism spectrum disorders (ASD; Yamada et al., 2007; Cassidy et al., 2008; Hamlyn-Wright, Draghi-Lorenz, Ellis, 2007; Herring et al., 2006; Hastings et al., 2005; Osborne, 2008; Siman-Tov, Kaniel, 2011; Johnson et al., 2011); yet, some families are able to be resilient and thrive in the face of these challenges, positively impacting on their child's developmental outcome (Milshtein et al., 2010; Oppenheim, 2011; Aitken, Trevarthen, 2001; Gerstein, Crnic, Blacher, Baker, 2009).

Objectives: In the present work we consider family structure and dynamics as a crucial component of such resilience. Within such perspective, our aim is to assess the quality of family interactions comparing three subgroups: ASD only child families, two children families with both siblings diagnosed with ASD, and two children families, with one ASD diagnosed child and one typically developing child.

Methods: In order to assess family interactions, we administered to 15 families (children's mean age= 6.76, s.d.= 2.8; mothers' mean age= 38.9, s.d.= 5.4; fathers' mean age= 42.48, s.d.= 1.07) the Italian adaptation of the *Lausanne Triologue Play - LTP* (Fivaz-Depeursinge, Corboz-Warner, 1999; Malagoli Togliatti, Mazzoni, 2006). Degree of coordination partners achieve in seeking playful affective contact defines a 'family alliance', ranging from functional (*Cooperative alliance* and *Stressed alliance*) to problematic (*Collusive Alliance* and *Disordered alliance*). To evaluate the potential for parental behaviour problems and child adjustment difficulties within the family

system, we applied the *Parenting Stress Index - PSI* (Abidin, 1995).

Results: Overall, no family showed a collaborative alliance. However, 42.9% showed a functional, yet stressed alliance. Within dysfunctional alliances, 38.1% were collusive and 19% disordered. Student's t-tests showed significant differences between the quality of family relationships (LTP) and levels of parental stress (PSI) with respect to the number of ASD diagnosed children in the family. The less coordinated families were among families with both siblings diagnosed with ASD ($p= 0.001$). Nevertheless, the child's worst score on LTP was among the ASD only child families ($p=0.001$), whose parents also showed the highest level of stress ($p= 0.008$).

Conclusions: Results highlight the impact of Autism Spectrum Disorders on family ability to cooperate and on parental levels of stress and point out the relevance to include the whole system within the intervention program in order to enhance a positive environment and improve mental health and wellness of the family.

113.025 25 The Double ABCX Model of Family Adaptation in Families of Children with ASD Attending Early Intervention. J. M. Paynter*¹, E. Riley¹, W. Beamish² and M. Davies², (1)AEIOU Foundation, (2)Griffith University

Background: Families of children with ASD experience greater levels of individual distress and reduced family functioning relative to families of children who are typically developing (e.g., Lee, 2009), have another disability (e.g., Eisenhower, Baker, & Blacher, 2005), or who have a child with a chronic illness (e.g., Bouma & Schweitzer, 1990). The Double ABCX model of Family Adaptation (McCubbin & Patterson, 1983) has been used to conceptualize and organize the factors which may underlie such outcomes following diagnosis (Stuart & McGrew, 2009), at school age (Manning, Wainwright, & Bennett, 2010), and across a childhood sample (Bristol, 1987). These studies suggest a significant proportion of the variance in outcomes for the family system is explained by components of this model. To date however, no research has investigated this model's applicability to a key period, while the child with ASD is attending early intervention. Such research has important theoretical and practical implications in better

conceptualizing both the modifiable and fixed factors which affect family outcomes during their child's early intervention.

Objectives: The current study sought to investigate the applicability of the Double ABCX Model of Family Adaptation to families of children with ASD attending early intervention through investigating the links between model components and family outcomes. The outcomes investigated included individual impact (mood symptoms and parenting stress), relationship quality, and impact on family. It was predicted based on the model, that family systems outcomes would be linked to child symptoms (ASD symptoms and challenging behavior), pile-up of demands, internal resources (self-esteem), external resources (social support), appraisals, and coping strategies.

Methods: Participants included 43 parents (18 males, 25 females) of children aged 2½ to 6 years ($M = 49.35$, $SD = 9.21$ months; 8 female, 35 male) with an ASD who were attending an early intervention service. Participants completed questionnaire packets of standardized measures assessing constructs of the Double ABCX Model.

Results: As predicted by this model, family systems outcomes (individual, relationship and family) were linked to pile-up of demands, self-esteem, social support, appraisals, and coping strategies. Children's reported level of challenging behavior was also linked with individual outcomes (both mood symptoms and parenting stress) and negative impact on families, although it was not significantly linked to relationship burden. Level of ASD symptoms was linked only to parenting stress and negative impact on families, but not to mood symptoms or relationship burden.

Conclusions: This study provides preliminary support for the applicability of the ABCX model to families with children attending early intervention with the majority of hypothesized links between predictors and outcomes supported. Further research with larger samples is needed to investigate the relative contribution and relationships between predictor variables, as well as longitudinal or intervention studies to test the direction of effects. Such research has important practical implications for identifying fixed (e.g., gender) and modifiable (e.g., coping strategies) factors which may be indicators of needs, or

targets for interventions and services to better support families of children with ASD during their child's early intervention.

113.026 26 Longitudinal Change in the Use of Services in Autism Spectrum Disorder: Understanding the Role of Child Characteristics, Family Demographics, and Parent Cognitions. M. Siller*¹, N. M. Reyes², E. R. Hotez³, T. Hutman⁴ and M. Sigman⁴, (1)*Hunter College of the City University of New York*, (2)*Virginia Tech*, (3)*The Graduate Center of the City University of New York*, (4)*University of California, Los Angeles*

Background: Despite emerging consensus about many features of effective intervention programs (NRC, 2001; Odom et al., 2010), little information is currently available about the nature and intensity of services children with ASD typically receive in their local communities.

Objectives: The aim of this study was to examine child characteristics (i.e., gender, age, nonverbal cognitive and language abilities, ASD symptoms), family demographics (i.e., family composition, ethnicity/race, income, parental age, parental education, socioeconomic status), and parent cognitions (i.e., parenting stress, parenting sense of competence, parental concepts of development), that may affect access to early intervention, special education, and related services.

Methods: The sample included 70 children with ASD (chronological age: $M = 57$ months; $SD = 12$) who had limited expressive language abilities (expressive language age: $M = 16$ months; $SD = 9$). At baseline, children participated in comprehensive assessments to confirm ASD diagnosis (i.e., ADOS-G, ADI-R) and evaluate development (i.e., Mullen Scales of Early Learning). All parents were enrolled in a short education program, providing each parent with basic information and resources on advocating for a young child with ASD (Parent Advocacy Coaching, PAC). Over a period of four months, parents participated in four educational sessions, held in the families' home (one session per month, 90 minutes per session). Longitudinal change in children's intervention programs in the community was evaluated over a period of about 27 months, starting 12 months prior to enrollment in PAC. Data for this study were collected in the context of a clinical trial, evaluating a parent-

mediated intervention supporting parent-child communication (Siller et al., 2012).

Results: Data were analyzed by fitting a series of multilevel models for longitudinal data (SAS Proc Mixed; Singer et al., 2003). Results revealed large individual differences in the intensity of children's individual and school based services. Despite this variability, only two child characteristics (age, gender) emerged as independent predictors. In contrast, the intensity of children's intervention program was independently predicted by a broad range of demographic characteristics, including parental education, child ethnicity and race, and family composition. Finally, even after child characteristics and family demographics were statistically controlled, results revealed associations between specific parental cognitions (parenting efficacy, understanding of child development) and the subsequent rate of change in the intensity of children's intervention programs.

Conclusions: It is important to emphasize that this is not a study of the outcome of a given form of treatment (i.e., PAC). For such a study, one would need an appropriate control group of families who were not receiving the treatment in question. This being said, by ensuring that a minimum level of advocacy-support is available to all research participants, this research design is ideally positioned to identify factors that predict which families will be able to utilize available supports.

113.027 27 Neuromodulation with TMS Effects On Heart Rate Variability in Children with Autism. M. K. Hensley*, E. M. Sokhadze, A. S. El-Baz and M. F. Casanova, *University of Louisville*

Background:

Autism spectrum disorder (ASD) is a pervasive developmental disorder marked by difficulty in social interaction, lack of communication, and restricted range of interests. Many children with autism exhibit symptoms associated with autonomic dysfunction. The main findings of autonomic abnormalities studies in autism point at reduced parasympathetic activity in association with increased sympathetic tone resulting in autonomic disbalance which affects physiological functions and manifests in heart rate variability (HRV) measures.

Objectives:

Objective of the study was to investigate cardiac rhythm measures reflecting autonomic nervous system activity in children with autism undergoing treatment using 1 Hz repetitive Transcranial Magnetic Stimulation (rTMS). Our hypothesis was that as weekly rTMS sessions continued, individuals would display a decrease in heart rate (HR) and increase in HRV, indicative of enhanced parasympathetic nervous system activity and/or decreased sympathetic activity.

Methods:

Twenty individuals with ASD were enrolled in the study. EKG-based HR and HRV were recorded with a C-2 J&J monitor. HR analysis was done using Kubios software. We investigated changes in HR and HRV during rTMS course with 18 weekly sessions.

Results:

Post-rTMS outcomes showed slower HR accompanied by decrease of low frequency (LF), increase of high frequency (HF) component of HRV, and lower LF/HF ratio. Our findings show reduced sympathetic activation after TMS resulting in lower HR predominantly through withdrawal of sympathetic tone (LF of HRV) rather than increase of parasympathetic (vagus) cardiac neural control activity post 12 rTMS sessions, but higher HF component after 18 sessions.

Conclusions:

Prefrontal rTMS activates inhibitory tone of the frontal cortex resulting in a lower excitation of the autonomic system probably through the inhibitory fronto-limbic circuits. We found that weekly rTMS sessions increase parasympathetic nervous system activity and decrease sympathetic nervous system activity, and is therefore a promising candidate for treatment of ASD.

113.028 28 Teacher Burnout Predicts Child Goal Attainment Outcomes. L. A. Ruble*¹ and J. H. H. McGrew²,
(1)*University of Kentucky*, (2)*Indiana University - Purdue University Indianapolis*

Background:

Special educators experience higher attrition rates than general educators, as approximately 25% of special educators exit every three years (McLeskey & Billingsley, 2008). Furthermore, stress and dissatisfaction with their teaching positions lead an additional 20% to transfer to general education or seek another position in special education each year (Boe, Cook, & Sunderland, 2008). This turnover is so serious that many special education teachers are hired without adequate preparation (McLeskey & Billingsley, 2008). Over the past several decades, researchers have identified stress and burnout as major factors contributing to teacher turnover (Awa, Plaumann, & Walter, 2010). Burnout is described as the eventual consequence of chronic and long-term stress (Billingsley, 2004; Farber & Ascher, 1991). Students with specific disabilities that may be particularly challenging are those with autism spectrum disorders (ASD; Jennett, Harris, & Mesibov, 2003). Kokkinos and Davazoglou (2007) found that the majority of teachers indicated that teaching students with autism posed the most stress in comparison to teaching other groups of students with disabilities such as those with emotional or behavioral problems, ADHD, or cognitive disabilities. To date, most studies have documented the impact of burnout on teacher variables (e.g., retention), but no studies to our knowledge have examined the impact on student variables (educational outcomes).

Objectives:

To evaluate the impact of teacher stress and burnout on child educational goal attainment outcomes.

Methods:

Teacher stress and burnout data collected for another study was used for secondary analysis. A total of 73 special education teachers who taught preschool and elementary children with autism completed the Maslach Burnout Inventory (Maslach, Jackson, & Leiter, 1997) and the Index of Teaching Stress near the beginning of the school year. At the end of the year, student outcomes were measured by an independent observer using a psychometric equivalent goal attainment scale (PET-GAS) approach for three goals selected to assess improvement in student

skills representing ecologically and socially valid goals reflected in the Individual Education Programs (IEPs; Ruble, McGrew, & Toland, 2012). Change scores were calculated by subtracting end of year PET-GAS scores from beginning of the year scores. Intercorrelations between PET-GAS, teacher burnout, and stress were calculated.

Results:

Student outcomes were lower for teachers reporting increased emotional exhaustion ($r = -.20, p < .05$) and stress ($r = -.21, p < .05$) at Time 1 (see Table 1).

Table 1. Intercorrelations between Student Outcome and Teacher Burnout and Stress

| | GAS | MBI EE | MBI DEP | MBI PA | ITS |
|----------------|-------------------|--------------------|--------------------|--------------------|--------------------|
| PET-GAS Change | -- | -.20 [†] | -.09 | .13 | -.21 [†] |
| MBI-EE | -.20 [†] | -- | .49 ^{**} | -.44 ^{**} | .29 ^{**} |
| MBI-DEP | -.09 | .49 ^{**} | -- | -.35 ^{**} | .28 ^{**} |
| MBI-PA | .13 | -.44 ^{**} | -.35 ^{**} | -- | -.41 ^{**} |

Note. PET-GAS: Psychometric equivalence tested goal attainment change score; MBI: Maslach Burnout Inventory (EE: emotional exhaustion; DEP: depersonalization; PA: personal accomplishments); ITS: Index of Teaching Stress

Conclusions:

This is the first study showing a direct and predictive relationship between teacher stress and burnout and child educational outcomes. Further work is needed to understand exactly what aspects of teaching are affected and to identify methods to mitigate burnout and impact on the student.

113.029 29 Training for Educators of Students with Autism Spectrum Disorders. A. P. Juárez*¹, C. M. Taylor¹, L. Garrett¹, W. A. Loring², K. H. Frank¹, E. Carter², M. Brock², H. Huber², E. Wallace¹, A. Stainbrook¹, S. Blumberg¹ and Z. Warren¹, (1)Vanderbilt Kennedy Center, (2)Vanderbilt University

Background: Given a prevalence of 1 in 88 (CDC, 2012) there is an increasing need for both

general education and special education teachers and affiliated staff to be knowledgeable and skilled in implementing evidence-based teaching strategies for students with ASD. Research indicates that teachers are not sufficiently trained to work with students with ASD through teacher preparation programs (Scheuermann et al., 2003), even in states where autism-specific training is required (Loaicono et al., 2008). Furthermore, a variety of school personnel, including teachers, administrators and speech-language pathologists report inadequate training regarding working with students with ASD (Schwartz & Drager, 2008; Stahmer et al., 2005). In addition, research suggests that a majority of teachers are not utilizing evidence-based strategies to teach their students with ASD (Hess et al., 2007).

Objectives: In the current study we: 1) examined the effectiveness of training sessions offered to school personnel by an autism-specific professional development team and 2) we indexed the additional needs of the educational community not covered through this training approach.

Methods: In the initial phase of the study, participants (n=82) were school system employees attending autism-specific training sessions funded by the state department of education. Participants were general and special education teachers, paraeducators, speech-language pathologists, administrators, and autism and behavior consultants. Each participant completed a pre-session and post-session questionnaire, in which they rated their confidence in identifying characteristics of ASD and utilizing a variety of evidence-based strategies to teach students with ASD. In the second phase of the study, participants were school system employees from across a state in the southeastern United States. Participants were requested, via electronic mail, to complete a survey regarding their professional development needs in relation to students with ASD.

Results: Preliminary results indicate that autism and behavior consultants, special education teachers, and speech-language pathologists enter professional development sessions with the greatest initial ASD-specific knowledge. Paraeducators and administrators enter training with the least initial ASD-specific knowledge.

Overall, participants made significant self-reported gains in their ability to utilize behavioral and teaching strategies covered in the ASD-specific professional development sessions ($p < .01$ in all assessed areas of knowledge). General education teachers and paraeducators made significantly more gains in knowledge from pre-test to post-test than other groups ($p < .01$), particularly in their understanding of how to best organize a classroom to help a child be available for learning.

Conclusions: Training for school system employees appears to be an effective way to increase their knowledge and confidence in teaching and working with students with ASD. Further research needs to be conducted to identify specific training needs of educators of students with ASD. In addition, it is important to consider which learning modalities are most accessible and provide the best training opportunities.

113.030 30 "Read with Me!": The Effect of Dialogic Reading On Early Literacy Outcomes for Preschoolers with Autism. V. Fleury*, *University of North Carolina at Chapel Hill*

Background: Children's literacy development is believed to begin long before children receive formal reading instruction in elementary school. By participating in informal literacy activities early in life, such as adult-child storybook reading, children can develop a number of skills (i.e., oral language, print and letter knowledge, phonological awareness) that relate to later reading achievement (NELP, 2008; Snow, Burns, & Griffin, 1998; Whitehurst & Lonigan, 1998). Given that children with special needs are at high risk for reading difficulties (Landgren, Kjellman, & Gillberg, 2003), it is especially important that they receive repeated opportunities and appropriate supports to participate in literacy activities beginning in early childhood. However, educators may encounter a number of difficulties in their attempts to provide appropriate literacy opportunities for their students with disabilities. For children with Autism Spectrum Disorder (ASD), features that are characteristic of their disorder may further impede their ability to participate in literacy activities, placing them particularly at risk for reading problems. The

incorporation of dialogic reading techniques (Whitehurst & Lonigan, 2001) in adult-child book reading has been effective in improving early literacy skills in children with language delays and those from at-risk populations. There is, however, limited research that examines the potential utility of dialogic reading strategies for children with disabilities such as ASD.

Objectives: To determine the effect of dialogic reading on early literacy development in young children with ASD, specifically on children's (1) performance on formal measures of emergent literacy knowledge; (2) knowledge of vocabulary specifically targeted in books; and (3) participation during book reading.

Methods: In this study, a multiple baseline design across participants was used to examine the effect of a modified dialogic reading approach on early literacy outcomes in 14 preschool students with ASD. Baseline book reading sessions consisted of school personnel reading to students "as they would normally." Intervention book reading sessions consisted of school personnel reading to students using a modified dialogic reading approach.

Results: School personnel who served as interventionists were able to learn modified dialogic reading techniques and appropriately apply the strategies in daily book reading with their students. Results indicate that dialogic reading was effective in improving some components of early literacy skills for children with ASD, particularly oral language skills. Baseline book reading, in which school personnel read to students "as they would normally," resulted in consistently low levels of verbal participation by students followed by an immediate increase in verbal participation during dialogic book reading sessions. Children in this study also showed improved outcomes in book-specific vocabulary and listening comprehension skills during book readings that incorporated dialogic reading techniques. There were no differences found in phonological awareness and print concepts.

Conclusions: The results of this study suggest that the incorporation of dialogic reading strategies during shared book reading is effective in improving oral language outcomes and

participation in preschoolers with ASD. Dialogic reading is a promising practice that should be incorporated as a part of early literacy curriculum for children with ASD.

113.031 31 The Development of Early Literacy Skills Among Young Children with ASD: Predictors of Change Over Time Across Literacy Skill Domains. J. Blacher*¹, A. Eisenhower², L. A. Tipton³, S. Kaplan-Levy² and J. M. Wilson², (1)*University of California - Riverside*, (2)*University of Massachusetts Boston*, (3)*University of California, Riverside*

Background:

The development of literacy skills is a central goal of children's early school years, yet the literacy development of children with ASD is not well understood. Skills across the "Big Five" literacy domains may develop unevenly for children with ASD (Whalon & Hart, 2011); in particular, encoding may be a relative strength while comprehension may be a relative weakness for children with ASD (Nation et al., 2006). Too, there may be different pathways to literacy success for children with ASD compared to children with neurotypical development (Asberg et al., 2010).

In particular, social skills, and the ability to connect with teachers and learn from teacher-child interactions, are crucial to academic skill development (Pianta & Stuhlman, 2004). Among children with ASD, social-communicative functioning may be a particularly strong determinant of learning and literacy growth over time.

Objectives:

Our paper will present the profiles of literacy development in young children with ASD across five areas (vocabulary, encoding, fluency, alphabet knowledge, and comprehension) and trajectories of literacy performance across 1.5 years. We examine child characteristics that predict baseline literacy skills and change over time, as well as teacher qualities and aspects of classrooms and services that predict changes in literacy skills.

Methods:

Children ages 4-7 (80% boys) who meet criteria for autism or ASD on the ADOS and score at or above 50 on a brief IQ assessment are evaluated

four times over 1.5 years. Enrollment is underway (n=113 to date). Assessments of literacy include subtests of the Woodcock-Johnson Tests of Achievement, 3rd Edition and grade-level probes on the AIMSweb system.

Results:

Paralleling the wide IQ range in our sample, literacy skills also ranged widely. By the start of the school year, an aggregate profile was evident, marked by a relative strength in basic decoding skills (M=113.8, SD=18.3), a relative weakness in picture vocabulary (M=98.9, SD=13.9), and moderate performance in fluency (M=106.0, SD=16.4) and alphabet and word knowledge (M=109.6, SD=16.9). This profile was highly consistent 6 months later; reading comprehension was also age-appropriate (M=100.6, SD=17.4).

Consistent with non-ASD samples, 23-45% of the variances in literacy skills across domains were explained by child characteristics (here, IQ, language ability, ASD severity, behavior problems, and social skills). With regard to skill development over time, hierarchical regressions revealed that child cognitive ability predicted growth in vocabulary above and beyond baseline vocabulary, whereas higher baseline language ability predicted marginally greater growth in reading fluency. Interestingly, only social skills, but no other child characteristics, predicted unique growth in decoding skills.

Subsequent analyses with the complete sample will use structural equation modeling to examine change in literacy skills over time, including the relative contributions of teacher and classroom factors to literacy outcomes and the reciprocal associations between child characteristics and literacy outcomes over time.

Conclusions:

Preliminary results suggest that literacy development for children with ASD is impacted by distinct child characteristics that may differ from children without ASD. Discussion will address implications for school-based interventions aimed at psychosocial and academic adjustment for young children with ASD.

Neuropathology Program

114 Neuropathology

114.032 32 Genetics and Neurodevelopment of Agenesis of the Corpus Callosum: Insights for Autism. E. Sherr*, UCSF

Background: Recent studies suggest that up to 45% of children with agenesis of the corpus callosum (AgCC) have significant symptoms on the autism spectrum. In addition, there is considerable evidence linking subtle callosal anomalies to a larger percentage of autism spectrum disorder (ASD) patients.

Objectives: Identify the genetics of callosal agenesis and describe aberrant patterns of fiber pathways evident in these individuals.

Methods: We have used a wide array of genetic tools, including genome-wide copy number variant (CNV) analysis, linkage analysis, cloning of chromosomal breakpoints as well as high priority gene resequencing approaches. For analysis of the anatomic phenotype in patients, we have used diffusion tensor imaging with deterministic tractography and connectome analysis.

Results: We performed high-throughput genome-wide SNP arrays on a cohort of 275 individuals with AgCC and 2349 controls. Patients with AgCC had an enrichment of gene rich CNV >1 Mb ($p=6.10 \times 10^{-4}$; odds ratio [OR] = 5.22) and 9.4% of AgCC patients had a large de novo CNV. Rare AgCC CNV overlapped significantly with CNV genes in ASD and intellectual disability (ID) ($p=3.82 \times 10^{-3}$; OR=2.12 and $p=1.64 \times 10^{-3}$; OR=5.23 respectively), and were more linked when comparing de novo AgCC CNV to ASD and ID ($p=1.50 \times 10^{-3}$; OR=7.55 and $p=0.001$; OR=23.4 respectively). We have also shown that many of the identified CNV in this study overlap with chromosomal intervals identified in prior AgCC studies, highlighting the recurrence of AgCC genes. Overall, these findings underscore the genetic connection between AgCC and both ASD and ID and point to pathways implicated in these disorders. Additional results on single gene analyses (both published and recent work) will be presented. We have also investigated the hypothesis that additional white matter tracts that may accompany AgCC may be equally important for the ASD phenotype seen in AgCC individuals. Using deterministic tractography and targeted volumetrics, we have shown that the cingulum

bundle, as measured by volume and fractional anisotropy is reduced in size and in degree of microstructural integrity in AgCC individuals compared to matched controls. We also conducted a structural connectome analysis of AgCC patients in comparison to matched controls. To further this analysis, we compared AgCC patients to controls in which we have simulated removal of all callosal connections ("virtual callosotomy"). This investigation demonstrated that the network topology of AgCC is more variable than that seen in controls and that the degree of aberrant connectivity seen in AgCC is much more pervasive than can be explained simply by the absence of callosal fibers. Indeed, modularity analysis points to weak connectivity in the bilateral cingulum bundles, confirming our deterministic tractography analysis.

Conclusions: Our genetic findings demonstrate that the biology that underlies AgCC is highly linked to both ASD and ID and that de novo CNV are a significant cause of AgCC, Tractography and connectome analysis highlight changes in other white matter tracts present in AgCC patients and suggest that biological pathways implicated in CC development are shared by many white matter tracts throughout the brain and are thus important factors in the development of autism spectrum disorders.

114.033 33 The Primary Olfactory Cortex in Autism Spectrum Disorder. D. A. Menassa*, C. Sloan, C. Emin and S. Chance, *University of Oxford*

Background: Individuals with autism spectrum disorder (ASD) frequently have altered sensory sensitivity, including impairments in three olfactory-testing domains: olfactory identification, sensitivity and discrimination. The primary olfactory cortex, which is known anatomically as the piriform cortex (PiC), receives direct input from the olfactory bulb and is therefore a key structure in processing the sense of smell. Some alterations of this brain structure have been reported in mouse models (e.g. deficits in oxytocin-receptor expression in the reeler mouse). However, the human neuroanatomy of the PiC in ASD individuals has not been investigated.

Objectives: The aim of this study was to define the structure of the PiC with precision in post-mortem brains from 8 ASD and 10 control donors for qualitative neuropathological assessment and

quantitative investigation of glial, non-pyramidal and pyramidal cell densities in layers II and III of this brain area.

Methods: Subjects were selected from the Harvard, Maryland and Oxford Thomas Willis brain banks with appropriate ethical approval. Samples were age-matched. 25 um-thick sections were obtained from paraffin-embedded blocks and 5 sections per case were cut and stained with Cresyl Violet (0.1%) to visualise Nissl-substance for neuropathological assessment. A section sampling fraction of 0.125 was used and unbiased cell density measurements were performed.

Results: We found that, to obtain the characteristic Nissl-stained S-shape of the three-layered structure, the PiC needs to be sampled from the anterior side of the first coronal slice that shows the beginning of the temporal lobe at the level of the endorhinal sulcus. Detailed qualitative anatomical assessment revealed no overall microscopic neuropathology in the structure of the PiC in ASD brains. Dorsally, layer III of the PiC is anatomically bound by the claustrum, laterally by the limen insula and ventrally by the endopiriform nucleus of the anterior amygdala. Preliminary data from the stereological investigation provided estimates of the different cell sub-populations including pyramidal, non-pyramidal and glial cells in layers II and III of this structure. In layer II, the average cell densities were: pyramidal neurons- 171 ($\times 10^3$) cells/mm³, non-pyramidal neurons- 24 ($\times 10^3$) cells/mm³, glial cells- 62 ($\times 10^3$) cells/mm³. In layer III, pyramidal neurons averaged- 19.1 ($\times 10^3$) cells/mm³, non-pyramidal neurons- 3.1 ($\times 10^3$) cells/mm³, glial cells- 36 ($\times 10^3$) cells/mm³.

Conclusions: The PiC is unusual due to its three-layered structure and constitutes a novel area of investigation in ASD. We report no visible neuropathological anomaly of the microscopic organisation of the PiC by qualitative assessment. Further stereological measurements will reveal if the balance between the different sub-populations is altered and whether this might relate to the olfactory impairments seen in ASD individuals.

114.034 34 Autism BRAIN Stereology Project – 12 YEARS and Counting. J. A. Pickett*¹, P. R. Hof² and J. Wegiel³, (1)*Autism Speaks*, (2)*Mount Sinai School of Medicine*, (3)*New York State Institute for Basic Research*

Background: A fundamental part of brain banking is the neuropathologic examination of portions of 20 or more major brain regions, examined microscopically. In 2001, two investigators independently proposed projects that altered the processing and evaluation of brains by adding a stereology focus to examine whole brain hemispheres, not just selected portions. In the same year, a Neuropathology of Autism focus group recommended that post mortem brains be imaged (MRI) when possible. The interests culminated in a joint project funded by Autism Speaks titled Clinicopathological Correlations in Autism. It included MRI and comprehensive stereology of age- and gender-matched hemispheres.

Objectives: To find cellular correlates of gross alterations seen in the autism brain by *in vivo* imaging studies within a protocol of systematic stereologic study of whole hemispheres. The data will contribute to understanding the clinical course of autism as well as defining circuits that are amenable to pharmacological treatment. An important component of the Project is the availability of unstained sections and stained slides to other researchers and analysis of results reported by the participants. The early projection of the final subject cohort was 10 autism and 10 control hemispheres ranging from age 2 to 75.

Methods: The Project combines imaging techniques, computer-based image analysis, computer-based stereology (unbiased methods to estimate morphometric parameters such as number, density or volumes of cells), immunochemical staining of cell components, and neuropathology. Special attention is paid to donor phenotype with documentation of testing and medical histories of the donor and family. Collaborating laboratories image the formalin-fixed hemispheres, embedding in celloidin and sectioning ~seven hundred 200 μm -thick sections. One-third is stained with cresyl violet, 1/3 with galloxyanin, and the remaining 1/3 sections are preserved in ethanol; all are available upon request/approval by the ATP's Tissue Advisory Board. The two principal investigators explored the number, size, and spatial arrangement of neurons in the fusiform gyrus and the fronto-insular, anterior cingulate and inferior temporal cortices as well as the memory system

(entorhinal cortex, hippocampus, amygdala), the sensorimotor system (basal ganglia, nucleus accumbens, substantia nigra), cerebellum and brainstem. The research has been supported by a number of brain banks and funded by Autism Speaks, the author's institutions, NIH, and DOD grants since 2002.

Results: Forty-two hemispheres have been processed; 30 males and 12 females; 23 autism and 19 controls. With the best age-gender-laterality matching, there are 14 hemispheric pairs for the core comparative analysis. Imaging, cell counting, and neuropathologic examinations have been ongoing since 2001 with the target regions to be completed by the end of 2012. These data will be presented at IMFAR and made available of the ATP portal.

Conclusions: The Brain Atlas Project was conceived to provide information about the brains of males and females with autism relative to known pathological processes and also relative to unaffected control brains of the same maturation (age). The data serve as a baseline for further studies and will be of immediate importance to an additional 10-12 laboratories also studying this cohort.

114.035 35 Increased mGluR1 mRNA Subunit Levels in Purkinje Cells in the Crus II Cerebellar Hemisphere but Not Vermis in Autism: An *in Situ* Hybridization Histochemical Study. G. J. Blatt*, A. P. Piras and J. J. Soghomonian, *Boston University School of Medicine*

Background: In addition to activation of ligand-gated channels by the excitatory neurotransmitter glutamate, receptor activation also occurs via G-protein coupled metabotropic glutamate receptors (mGluRs) which signal to intracellular cascades. mGluRs are homomeric receptors with eight subtypes in three groups. Human cerebellar mGluR1 mRNAs in Group I, are normally highly expressed in the granule cell layer and in Purkinje cells (PCs) and have a lower signal in the molecular layer. Functionally, mGluR1s play an important role in synaptic signaling and modulating synaptic plasticity in the cerebellum. Glutamate transmission via mGluR1s in PCs result from the production of a complex postsynaptic response consisting of a local dendritic calcium signal from IP-3 receptor-mediated calcium release from internal stores and, the production of a slow excitatory

postsynaptic potential mediated by the novel transient receptor potential ion channel TRPC3.

Objectives: To determine whether there are alterations in PC mGluR1 mRNA levels in two distinct regions of the cerebellar cortex in autism cases relative to age- and postmortem-interval matched controls. The hypothesis is that there will be an increase in mGluR1 levels in the Crus II region of the lateral hemisphere in autism cases but normal levels in the vermis (centered on lobule VI). The rationale is that there have been more severe PC deficits and previously demonstrated GAD 67 mRNA changes in Crus II in autism cases.

Methods: *In situ* hybridization histochemistry and autoradiography were used to examine the cellular distribution of mGluR1 receptor subunit mRNA in the Crus II region and quantitative analysis of mGluR1 expression was obtained by measuring silver grain density in 120 Purkinje cell somata for each case from n=9 control and autism cases (Crus II) and n=8 control and autism cases (vermis). The age range was 16-39 years for autism and 17-43 years for controls. Grain density corresponding to mGluR1 mRNA labeling was expressed as a mean number of pixels per surface area using NIH Image J analysis software and two-tailed unpaired t-tests were applied to determine significance at a $p < 0.05$ level.

Results: Statistical analysis of PCs showed a significant increase in mGluR1 mRNA levels in the autism group compared with control in the Crus II area ($p = 0.0138$), representing a 27% mean increase in mRNA levels in the autism group relative to controls. In contrast, there was no significant difference in vermal lobule VI ($p = 0.2752$) between autism cases and controls.

Conclusions: The Crus II region, which receives strong input from the frontal lobe via the pons, and implicated in high order cognitive processes, contains PCs with significantly increased mGluR1 mRNA expression levels, suggesting excess activation of synaptic signaling and altered modulation of synaptic activity in the autism brain. Combined with previous findings of decreased GAD 67 mRNA levels in Crus II PCs in autism, these data suggest that there are imbalances in the excitation:inhibition ratios in the cerebellum that potentially influence its

functions in motor learning, timing and correction of movements and/or frontal lobe-related cognitive functions.

114.036 36 Age-Related Changes in Neuronal Populations in the Amygdala in Autism. N. Barger^{*1}, D. G. Amaral² and C. M. Schumann¹, (1)UC Davis MIND Institute, (2)University of California Davis Medical Center

Background: Investigations of autism neuropathology have highlighted neural dysfunction in regions of the brain that process social and emotional information. We have previously shown that one such structure, the amygdala, contains fewer neurons in autistic adults, due largely to decreases in its lateral nucleus. However, the MRI literature indicates that the autism phenotype is marked by irregular developmental trajectories, broadly, and in the amygdala, particularly.

Objectives: In order to assess whether lower neuron numbers in the amygdala of autistic adults may also be the product of irregular development, we extended our original stereological analysis, counting neurons in the amygdala using an expanded dataset with a greater focus on childhood.

Methods: We used the optical fractionator technique to estimate neuron number in Nissl-stained sections from a postmortem sample of autistic and control cases between 2-44 years of age. Data were divided into three age classes, child, adolescent, and adult, including at least 6 cases per class. A 2-way ANOVA and pairwise comparisons were used to assess the influence of age class and diagnosis on neuron number. Additionally, neuron numbers in each diagnostic group were regressed against subjects' numeric age, testing for the possibility of a linear, quadratic, or cubic relationship between variables.

Results: Children with autism exhibited a slightly higher mean number of neurons in the lateral nucleus than typically developing children, but this relationship was reversed in adolescence and adulthood. The 2-Way ANOVA approached significance. The main effect of age class did not reach significance, but the main effect of diagnosis and the interaction of age class and diagnosis approached significance. Specifically, pairwise comparisons indicated that the number of neurons in the lateral nuclei of autistic children

was significantly greater than in autistic adults ($p = 0.037$) and nearly significantly greater than in autistic adolescents ($p = 0.059$). In pairwise comparisons of diagnostic categories within discrete age classes, adults, but not children or adolescents, with autism exhibited significantly fewer neurons in the lateral nucleus compared with control cases ($p = 0.035$). No age differences were evident in the control sample. Reinforcing these trends, the relationship between numeric age and neuron number in autism was best described by a negative linear regression line ($p = 0.067$). Neuron number in control cases was not closely related to numeric age ($p > 0.50$ for all lines).

Conclusions: In our sample, autistic children exhibited approximately the same number of neurons in the lateral nucleus as control children, statistically, although autistic adults exhibited significantly lower numbers. This is presumably due to an age-related decrease in neuron number in autism, rather than age-related changes in control cases. These preliminary findings suggest that autistic individuals are not born with a deficit of amygdala neurons, but may experience greater rates of neuron loss through development than do typically developing individuals. The low availability of tissue in young age classes clearly limits statistical power in this and related developmental analyses, but our findings highlight the importance of assessing variation at the earliest stages of autistic neuropathology.

114.037 37 Antibodies Reacting to Brain Tissue in Basque Spanish Children with Autism Spectrum Disorder and Their Mothers. C. C. Rossi^{*1}, J. Fuentes², J. Van de Water³ and D. G. Amaral⁴, (1)*University of Colorado Anschutz Medical Campus*, (2)*Policlinica Gipuzkoa*, (3)*The M.I.N.D. Institute, University of California, Davis*, (4)*University of California Davis Medical Center*

Background: Previous investigations found that a subset of children with autism spectrum disorder (ASD) in California possessed plasma autoantibodies that reacted intensely with brain interneurons or other neural profiles. Moreover, for several cohorts of American women, maternal autoantibody reactivity to specific fetal brain proteins was highly specific to mothers of children with ASD.

Objectives: We sought to determine whether children with ASD and their mothers from a

regionally specific cohort from the Basque Country of Spain demonstrated similar reactivity.

Methods: Thirty-seven subjects with ASD from Gautena (the regional program for ASD in the Gipuzkoa province of Spain) and 37 typically developing matched subjects from the local schools participated, along with the mothers of each subject and siblings of children with ASD. Children's samples were immunohistochemically reacted in California with sectioned rhesus macaque brain tissue, and plasma IgG reactivity to brain proteins was measured using western blot technology. Plasma samples were processed and evaluated in an identical manner to what was done in previous studies.

Results: Plasma from 22% of subjects with ASD and 19% of typically developing controls reacted to brain interneurons. One subject with ASD and one control subject displayed plasma reactivity to brain nuclei (representing 3% of subjects in both groups), and plasma from one subject with ASD reacted to beaded axons. No difference in the occurrence of brain reactivity was observed between subjects with and without ASD. Siblings of children with ASD were screened for ASD and each received a score below the cutoff that would indicate a suspicion of ASD. They did not differ significantly from children with ASD or typical controls with respect to plasma reactivity to cerebellar proteins. Five percent of maternal samples from mothers of children with ASD reacted to fetal brain proteins at 37 and 73 kDa, and 3% of samples from mothers of children with ASD reacted to fetal brain proteins at 39 and 73 kDa. These combinations were exclusively observed in mothers of children with ASD. While the occurrence of these two combinations did not differ significantly between the two maternal groups in the current study, the findings are consistent with previous studies (in which reactivity to these combinations was exclusively found in mothers of children with ASD) that did reach significance.

Conclusions: Reactivity of children's plasma samples did not differ based on a diagnosis of ASD. The percentage of children in the Spanish sample (both with and without ASD) whose plasma reacted intensely with interneurons was the same as that observed in a recent analysis of American children enrolled in the Autism Phenome

Project, but was lower than an earlier American sample of similarly aged subjects. A comparison of the current findings with several previous studies with regard to maternal plasma immunoreactivity suggest that two combinations of reactivity – to proteins at 37 and 73 kDa or 39 and 73 kDa – are specific to mothers of children with ASD across different populations.

114.038 38 Abnormalities in Raphe Nuclei of Autistic 5 to 15 Year Old Subjects. J. Wegiel*¹, E. C. Azmitia², T. Wisniewski³ and P. Banerjee¹, (1)*The College of Staten Island (CUNY)*, (2)*New York University*, (3)*New York State Institute for Basic Research in Developmental Disabilities*

Background: Serotonin is one of the first neurotransmitters to appear in the brain and has been considered as a developmental signal in cell proliferation, differentiation, and apoptosis (Whitaker-Azmitia 1991, Azmitia 2001, Verney et al. 2002). The role of the serotonergic system in autism is supported by more than 500 reports. They reveal a link between serotonergic system alterations and social deficits, repetitive behavior, hyperactivity, anxiety and obsessive compulsive behavior (Buitelaar and Willemsen-Swinkels 2000). An increase in the serotonin level in the blood platelets is often observed in autism (Hranilovic et al. 2007, Melke et al. 2008). The correlation between increased blood serotonin level and clinical severity supports the clinical relevance of hyperserotonemia in autism (Hérault et al. 1996). Brain imaging demonstrates serotonergic system impairment and the link between brain serotonin deficit and severity of social deficits in autism (Chugani et al. 1997, 1999; Makkonen et al. 2008). However, in spite of evidence of altered development of brain serotonergic system and contribution of these alterations to the autism phenotype, the raphe nuclei which are the source of brain serotonin have not been examined.

Objectives: The aim of the stereological and quantitative immunofluorescence-based study of raphe nuclei in autistic subjects 5 to 15 years of age and age matched control subjects was (a) to establish methods of brainstem preservation and unbiased raphe nuclei quantitative evaluation, and (b) to characterize the pattern of developmental abnormalities which may contribute to autistic phenotype.

Methods: Preliminary evaluation of brainstem samples revealed that during routine brainstem dissection with midsagittal cut in the midline and transverse cut on the level of the substantia nigra, raphe nuclei are partially or completely lost. From 9 autistic and 6 control subjects only 4 pairs 5 to 15 years of age were qualified for the study of raphe nuclei. Formalin-fixed brainstem was dehydrated and embedded in polyethylene glycol and cut into serial 50- μ m-thick sections. They were stained to estimate cell volume, and immunostained and examined in fluorescence to estimate amount of tryptophan hydroxylase reflecting serotonin synthesis level.

Results: 3-D reconstruction demonstrates topography and size of raphe nuclei and explains why preservation of raphe nuclei located in the midline requires modification of brainstem sampling. Nucleator (Microbrightfield) applied to cresyl violet stained sections revealed 24% smaller neuronal soma volume in the dorsal raphe nuclei of autistic subjects than in control group. Application of immunofluorescence and ImageJ software (NIH) revealed significant increase in tryptophan hydroxylase immunofluorescence in spite of smaller size of raphe neurons.

Conclusions: These data indicate developmental impairment of neuron growth comparable to that observed in cortex and in subcortical structures (Bauman and Kemper 1996; Casanova et al. 2006). Enhanced tryptophan hydroxylase immunofluorescence in raphe neurons is consistent with enhanced immunoreactivity in serotonergic fibers in several brain regions of autistic subjects (Azmitia et al. 2011). Pathology detected in raphe neurons suggests that target brain areas are exposed to altered levels of serotonin that may modify function of cerebral cortex and subcortical structures and contribute to the autistic phenotype.

114.039 39 Global Pattern of Delayed and Desynchronized Neuron Growth in the Brain of Autistic Subjects. J. Wegiel*¹, M. J. Flory², I. Kuchna¹, K. Nowicki¹, H. Imaki¹, J. Wegiel¹, I. L. L. Cohen², E. London², T. Wisniewski¹ and W. T. Brown³, (1)*New York State Institute for Basic Research in Developmental Disabilities*, (2)*NYS Institute for Basic Research in Developmental Disabilities*, (3)*NYS Institute for Basic Research in DD*

Background: The abundance of research focused on the cortex has resulted in a mainly

corticocentric theory of autism [Frith 2004, Geschwind and Levitt 2007]. However, the three diagnostic domains of autism engage subcortical structures including (a) the amygdala, involved in processing social information, emotional interpretation, fear, and anxiety [Amaral et al 2003, Baron-Cohen et al 1999, Winston et al 2002]; (b) the thalamus, involved in language functions, attention, anxiety and obsessive thinking [Ojemann and Ward 1971, Oke et al 1978]; (c) the striatum, linked to repetitive motor behaviors, compulsions and rituals [Day and Carelli 2007]; and (d) the brainstem and cerebellar deep nuclei, integrating a cerebellar role in motor functions, language and cognition, and eye motion control [Leyung et al 2000].

Objectives: The aim of this study was to test the hypothesis that subcortical structures are affected by developmental alterations and contribute to global brain developmental alterations and resulting functional deficits in autism.

Methods: To test this hypothesis of delayed and desynchronized growth of neurons in early childhood, the neuronal volume in 16 brain subcortical structures, the cerebellum and the archicortex was compared between autistic and control subjects of 4 to 8 years of age. Nineteen subregions (layers, sectors, nuclei) were examined to detect signs of desynchronized neuronal growth within individual anatomical brain subdivisions. To test the hypothesis that developmental defects of early childhood are partially corrected in late childhood and adulthood, the volume of neurons in the 4- to 8-year-old individuals with autism was compared with that of 9- to 64-year-old subjects with autism. Formalin fixed brains were dehydrated, embedded in celloidin, cut into 200- μ m thick serial sections and stained with cresyl violet. The volume of the neuronal soma and the nucleus was estimated by using Nucleator. The volume of brain structures was estimated with the Cavalieri method and the number of neurons with the dissector.

Results: A significant deficit of neuronal soma volume ($p < 0.001$) was detected in 89% of the structures examined, including all 16 brain structures and 15 of 19 of their anatomical subdivisions in 4-8 year old children with autism. Finding a very severe volume deficit in 17%,

severe in 44%, moderate in 22% and mild in 17% of the brain structures examined of the autistic subjects, we interpret as being a sign of desynchronized development of anatomically and functionally related neurons. This may help to explain the social and communication deficits, and the restricted repetitive and stereotypical patterns of behavior seen in autism. Finding a reduction of the developmental deficit from an average 19.6% in the 4-8 year old subjects to 8.8% in the over 8 year old subjects, suggests a delayed acceleration of the growth of neurons in late childhood and adulthood.

Conclusions: Brain region-specific neuron volume deficits may reflect desynchronized growth of neurons and neuronal networks in autism. The most severe delay seen in the 4-8 year old autistic children suggests that dysregulation of brain development before the 4th year defines autism encephalopathy and leads to dysfunction for life.

114.040 40 Lack of Focalization of Distant Connectivity with Attentional Engagement in ASD Children. C. J. Vaidya^{*1}, X. You¹, M. Norr¹, E. R. Murphy¹, W. D. Gaillard² and L. Kenworthy³, (1)*Georgetown University*, (2)*Children's National Medical Center*, (3)*Children's National Medical Center*

Background: Atypical functional connectivity (FC) particularly between long-distant regions, is posited to be a key pathology in Autism Spectrum Disorder (ASD). FC is measured by temporal correlations across regions during functional magnetic resonance imaging (fMRI). While many studies highlight long-distant underconnectivity in ASD, overconnectivity has also been observed (Müller et al., 2011). The mixed findings cannot be reconciled in the present literature as studies differ on multiple factors including methodological, subject characteristics, and task states (resting, cognitive task).

Objectives: FC may be atypical in ASD children, not only with respect to overall strength, but also in a failure to change in response to cognitive state. This has never been examined in ASD. Thus, we examined both local and long-distant intrinsic FC in two cognitive states (resting vs. sustained attention) in the same ASD and control children, using a data-driven voxelwise approach (Sepulcre et al., 2010). Further, we examined whether the state-related change in FC predicted

attentional function in everyday life measured by ADHD Rating Scale (DuPaul et al., 1998).

Methods: 15 9-13 year old ASD and 16 age, gender and IQ matched control children underwent fMRI (3mm isotropic resolution, TR 2000ms, TE 30 ms, flip angle 90°, FOV 192x192 mm) during rest and an attention task (Zink et al., 2003). Images were motion corrected by scrubbing (Power et al., 2011), slicetime corrected, normalized and resliced to 4mm, smoothed with 4mm FWHM, low pass filtered (<0.08Hz) and physiological noise removed. Time course of each voxel was correlated to every other voxel and thresholded at $p = .001$ FDR corrected ($r > .32$). FC maps were computed by averaging, for each voxel, the r -to- Z Fisher transformed values for voxels inside (local) and outside (distant) of 14 mm radius. Group (ASD, Control) X state (rest, task) interaction was examined for local and distant FC at $p < .001$, 5 voxels ($p < .05$ Monte Carlo corrected) covarying out age and motion.

Results: No interaction was observed for local FC. Changes in distant FC in frontal [left superior orbital frontal gyrus, Supplementary Motor Area (SMA), left Middle Frontal Gyrus (MFG - covering BA 10,6,8,9,44) and parietal (right paracentral lobule, right angular gyrus, left Temporal-Parietal Junction (TPJ)] lobes in response to sustained attentional engagement differed between ASD and control children such that distant FC strength was reduced (became more focal) in control children but increased (became more diffuse) in ASD children. Increased task-related distant FC may be maladaptive as the amount of increase in left superior orbital frontal gyrus, left MFG (BA 8,9,10,44), and SMA regions predicted inattention in everyday life in ASD children.

Conclusions: Group differences in FC of frontal and parietal cortex to the rest of the brain depended upon cognitive state. During the task, focalization of FC in control children may reflect selective engagement of task relevant networks whereas more diffuse FC in ASD children may reflect indiscriminate network engagement, perhaps leading to worse attentional function.

Brain Imaging Program
115 Brain Imaging - Structural

115.041 41 Abnormalities in Inter-Hemispheric Cortical Thickness Correlations in ASD. B. Khundrakpam^{*1}, J. D. Lewis¹, R. J. Theilmann², J. Townsend² and A. C. Evans¹, (1)McGill University, (2)University of California, San Diego

Background: Converging evidence from structural and functional neuroimaging studies points to disrupted connectivity in autism spectrum disorder (ASD), specifically reduced long-range connectivity (Just et al. 2004). But, the implications of this under-connectivity in terms of brain organization remain unclear.

Correlations in cortical thickness have been shown to be useful in distinguishing controls from individuals with Alzheimer's Disease (He et al. 2008), Schizophrenia (Bassett et al. 2008) and Multiple Sclerosis (He et al. 2009), and offer additional information with respect to cortical organization. To our knowledge, there are, to date, no studies of cortical thickness correlations patterns in ASD.

Objectives: We hypothesized that the cortical thickness correlation networks would show prominent changes in ASD, specifically in inter-hemispheric brain regions, as the corpus callosum has been shown to be reduced in ASD (Frazier and Hardan 2009). Through analysis of the cortical thickness correlation patterns in ASD, we seek to provide additional insight into the impact of the long distance under-connectivity on brain organization.

Methods: T1-weighted scans were collected from 22 male adults with ASD (34.14 ± 10.67 years) and 22 male controls (31.68 ± 8.75 years). CIVET, a fully automated structural image analysis pipeline developed at the Montreal Neurological Institute, was used to construct gray- and white-matter surfaces for each subject (Kim et al 2005). The distance between these surfaces was computed at 81,924 points; this was the measure of cortical thickness. The automated anatomical labelling (AAL) template, a commonly used atlas (Tzourio-Mazoyer et al. 2002), was used to parcellate cortex into 78 regions, and mean cortical thickness in each region was computed and used in the analysis. Correlations in cortical thickness between AAL regions were obtained for ASD and controls after controlling for age within each group. The resultant correlation matrices were z -transformed and group comparisons were done for the normal and ASD groups.

Results: Analysis of correlations in cortical thickness showed prominent changes in inter-hemispheric brain regions for the ASD as compared to the control group, but no significant difference in correlations for the intra-hemispheric brain regions. Group comparisons after z-transformation showed significantly increased correlations in several inter-hemispheric cortical regions.

Conclusions: Our results of increased correlations in several inter-hemispheric cortical regions in ASD as compared to normals might point to a suboptimal brain organization in ASD. In normal adults, inter-hemispheric cortical regions which are anatomically connected via the corpus callosum exhibit weak correlations in cortical thickness, possibly reflecting hemispheric lateralization. The inter-hemispheric under-connectivity that has been shown in ASD suggests abnormal lateralization. The overall increased cortical thickness correlations across inter-hemispheric cortical regions suggest that this abnormal lateralization takes the form of greater duplication of function between hemispheres.

115.042 42 Atypical Rightward Lateralization of the Corpus Callosum Is Present in Males but Not Females with Autism. D. L. Floris^{*1}, L. R. Chura², R. Holt¹, J. Suckling³, S. Baron-Cohen³ and M. D. Spencer³, (1)*Autism Research Centre*, (2)*Cambridge University*, (3)*University of Cambridge*

Background:

Rightward cerebral lateralization has been suggested to be involved in the neuropathology of autism spectrum conditions. In particular, corpus callosum volume is related to functional and structural brain asymmetries and due to its topographic organization might show lateralized morphology itself. Atypical patterns of cerebral lateralization might therefore be part of the pathophysiology of autism. Here we test if this is true in both males and females with autism, and whether this is true in siblings of people with autism.

Objectives:

To investigate whether rightward cerebral lateralization is (a) more common in adolescents with autism compared to their unaffected siblings and typically developing controls, (b) correlated

with clinical measures of symptom severity and (c) different in males and females with autism. We predicted, that in view of the "left hemisphere dysfunction" theory, in autism stronger rightward lateralization would be associated with more severe psychological deficits. We had no predictions in relation to sex as this was an exploratory study. Finally, if atypical lateralization is part of the "broader autism phenotype" it should also be present in the siblings of people with autism.

Methods:

Participants comprised adolescents with autism (males=35; females=17), their unaffected siblings (males=12; females=28) and typically developing controls (males=20; females=20) aged 12-18 years. We assessed functional asymmetry in terms of handedness using the Edinburgh Handedness Inventory and neuroanatomical lateralization in terms of corpus callosum asymmetry through manual tracing. Symptom severity was assessed using subdomains of the ADI-R and ADOS-G.

Results:

Male adolescents with autism showed stronger rightward lateralization in the posterior and anterior midbody the more left-handed they were, compared to controls. There were no significant differences in females with autism. In both sexes, symptom severity was related to rightward asymmetry in several subregions (splenium, isthmus, posterior midbody and rostral body). However the same directional associations occurred with different symptoms in the two sexes (males: repetitive and stereotyped behaviours (ADOS D), abnormalities in reciprocal social interaction (ADI A, ADOS B); females: communication problems (ADOS A), social interaction difficulties (ADOS B), abnormal play & imagination (ADOS C)). We did not find similar results in sibling pairs.

Conclusions:

Atypical rightward lateralization is present in males but not females with autism. This sex difference within autism might account for established sex differences within prevalence and

clinical phenotype and suggest the need for sex-specific diagnostic criteria. The dependence of atypical rightward lateralization on hand-preference highlights the link between function and anatomy. Siblings showed no similar pattern suggesting that atypical lateralization is a marker of autism per se, rather than the broader autism phenotype. Within groups, rightward lateralization has clinical relevance in both sexes. Future research should focus on the meaning of handedness and corpus callosum morphometry as a potential marker of clinical subgroups.

115.043 43 Shared Versus Specific Voxel-Wise Volumetric Characteristics in a Pair of Monozygotic Twins Discordant for ASD Traits. K. Mevel^{*1}, P. Fransson², P. Lichtenstein¹, H. Anckarsäter³, H. Forssberg¹ and S. Bölte¹, (1)*Karolinska Institutet*, (2)*Karolinska University Hospital*, (3)*University of Gothenburg*

Background: Comparison of monozygotic (MZ) twins discordant for Autism Spectrum Disorders (ASD) appears to be a promising lead to unravel the relative contributions of genetics and environment. However, studies investigating such populations are still scarce and mostly using the observer-dependent regions-of-interest approach to explore brain volumetry.

Objectives: To examine voxel-wise gray matter (GM) volumetry within a pair of MZ twins discordant for ASD traits versus typically developed controls, as a part of the Roots of Autism Twin Study Sweden ("RATSS").

Methods: The ASD traits discordant twins pair were 16;5 years old right-handed males, sharing several psychiatric comorbidities (dyslexia, dyscalculia, ADHD) and scoring 98/88 (Co-Twin1) and 99/84 (Co-Twin2) to verbal/perceptual IQ testing. Additionally, Co-Twin1 presented with marked autistic traits as assessed by both the Autism Diagnostic Observation Schedule (ADOS) and Autism Quotient (AQ), as well as tics. Six pairs of right-handed MZ twins were included as typically developed controls, with a median age of 16;4 (range: 12;6-18;3), median verbal/perceptual IQ of 106/109 and a male/female ratio of 4:8.

3T T1-SPGR data were processed in SPM8 as follows: i) unified segmentation (prior: NIHPD 13-18.5); ii) DARTEL with modulation and spatial normalization to MNI; iii) quantitative

normalization by the total intracranial volume (TIV); iv) smooth: 12mm FWHM. Additionally, an explicit mask was created from the mean of the modulated normalized GM maps. Thus, Co-twin1 and Co-twin2 final maps were subtracted from the controls' in order to obtain statistical maps reflecting the inter-individual differences. SnPM8b was used for statistical inferences, i.e. for One Sample t-tests testing for positive and negative effects in Co-twin1 and Co-twin2, using the GM mask and controlling for differences in sex and verbal/perceptual IQ. Results were considered as significant at $p \text{ FWE} < 0.05$, $k > 150$ voxels. Finally, individual values were extracted at each of the four most significant peak voxel pointed out by SnPM8b, to feed within-pairs Intraclass Coefficient (ICC) analyses.

Results: As compared to controls, both twins were characterized by lower TIVs, as well as GM volume i) increases in right medial (posterior cingulate) and lateral (supramarginal) parietal, and left temporal pole regions; ii) decreases in the left primary visual area. Co-Twin1 specifically showed increases in extended bilateral parietal regions, right inferior occipital, superior temporal and (orbito)frontal areas, and decreases in right inferior temporal, left orbitofrontal and middle occipital cortices. Right-lateralized increases (medial frontal, middle temporal, crus cerebellum) and decreases in right superior temporal, insula, visual associative cortex, and left primary somatosensory, medial and inferior temporal cortices were exclusively reported in Co-Twin2. ICC analyses highlighted the right superior temporal and medial frontal areas as being the regions showing the most significant differences between both twins, i.e. 72% and 47% increase when the discordant pair was excluded from the analyses, respectively.

Conclusions: For the first time, voxel-wise GM volumetric approaches are used to explore MZ twins discordant for ASD traits. Though they have to be cautiously considered, the findings pointed to differences in right superior temporal and medial frontal regions as potential neural substrates for differences in ASD traits.

115.044 44 Abnormal Functional Connectivity Is Associated with Disrupted Organisation of White Matter in Autism. J. McGrath^{*1}, K. A. Johnson², H. Garavan³, E. O'Hanlon⁴, A. Leemans⁵ and L. Gallagher¹, (1)*Trinity College Dublin*,

(2)University of Melbourne, (3)University of Vermont,
(4)Royal College of Surgeons in Ireland, (5)University
Medical Center Utrecht

Background: Autism spectrum disorders (ASDs) are devastating neurodevelopmental disorders of childhood of unknown aetiology. The theory of abnormal cortical connectivity holds that core features of ASD are underpinned by abnormal interregional brain connectivity. There is accumulating neuroimaging and genetic evidence supporting this theory; aberrant structural and functional connectivity has been widely reported, and genes involved in neural connectivity have been implicated as susceptibility genes for ASD. Previous work from our group has identified marked abnormalities of functional connectivity during visuospatial processing in ASD (McGrath et al, 2012, In Press, doi:10.1002/aur.1245). There is however a striking lack of research investigating the relationship between abnormal functional connectivity and white matter structure. In addition, the impact of aberrant neural connectivity on behaviour in ASD is poorly understood.

Objectives: The aims of this study were 1. to determine whether functional connectivity abnormalities were associated with structural abnormalities of white matter in ASD and 2. to examine the relationships between aberrant neural connectivity and behaviour in ASD.

Methods: Twenty-two non-medicated individuals with ASD and twenty-two age and IQ-matched controls completed a high-angular-resolution (61 directions) diffusion MRI scan. Structural connectivity was analysed using constrained spherical deconvolution (CSD)-based tractography, an advanced tractography method that avoids a number of critical confounds associated with traditional tensor based tractography. Seed regions for tractography were generated from functional connectivity maps during a visuo-spatial processing task that the same study group had completed (McGrath et al, 2012, In Press, doi:10.1002/aur.1245) and consisted of ten pairs of brain regions that showed abnormal functional connectivity in ASD. This tractography protocol allowed isolation of white matter tracts that directly connected brain regions showing abnormal functional connectivity. Fractional anisotropy (FA), a measure of micro-structural organisation of white matter, was

extracted from isolated white matter tracts. Correlation analyses were used to investigate the relationships between functional connectivity, structural connectivity and behaviour in ASD.

Results: CSD-based tractography revealed that there were white matter tracts directly connecting five of the ten seed-pair regions in most participants; between a seed region in the left occipital lobe (left BA19) and left caudate head, left caudate body, left uncus, left thalamus and left cuneus. FA in all five white matter tracts was reduced in the ASD group relative to controls, and this reduction was significant for white matter connecting the left BA19 and left caudate head, and left BA19 and left thalamus. In addition, there were significant correlations between structural and functional connectivity in the occipito-thalamic and occipito-striatal (caudate body) tracts, and between visuospatial processing speed and structural and functional connectivity measures.

Conclusions: This is the first study in ASD research to directly investigate how structural and functional connectivity are interrelated. Using an original approach integrating functional connectivity MRI and diffusion tractography, this work has revealed that abnormal functional connectivity in ASD is associated with disrupted organisation of white matter. This is particularly interesting as it provides novel evidence to suggest that structural brain pathology may contribute to the abnormal functional connectivity that has been widely reported in the autism literature.

115.045 45 Neuroimaging Findings in 16p11.2 Deletion and Duplication Carriers. P. Bukshpun*¹, N. Pojman¹, O. Glenn¹, J. V. Hunter², P. Mukherjee¹ and E. Sherr¹, (1)UCSF, (2)Baylor School of Medicine

Background: As a group, the reciprocal 593 kb 16p11.2 deletions and duplications are some of the most common genetic causes associated with autism, schizophrenia and other neurodevelopmental disorders. The Simons Variation in Individuals Project (Simons VIP) has enrolled nearly 200 individuals with a 16p11.2 deletion or duplication many of whom have undergone structural and functional brain MR imaging and a comprehensive phenotypic assessment including a neuropsychological battery, interviews, and clinical evaluations.

Herein we report findings from a qualitative assessment of the MRI visible neuroanatomical differences present in the 16p11.2 deletion/duplication population.

Objectives: We hypothesize that individuals with 16p11.2 deletions/duplications will have structural changes visible on brain MRI, and that many of these findings will differ between 16p11.2 duplications and deletions.

Methods: We reviewed high quality MRI scans of 66 deletion and 56 duplication carriers and 44 non-carrier family members using a structured review process targeting developmental anomalies. The reported findings represent the initial review of the project's lead board certified neuroradiologist blinded to genetic status. Frequencies of abnormalities were compared between deletion and duplication carriers and non-carrier family members using the Chi-squared test for independence, and significant findings surviving Bonferroni correction for multiple comparisons are presented.

Results: Several aberrant anatomical features were identified in patients with 16p11.2 deletion/duplications. When compared to non-carriers, 16p11.2 duplication patients showed an increased frequency of thin or dysmorphic corpora callosa (22% of patients, 2% of controls, $p < 0.01$), increased frequency of enlarged ventricles (25% of patients, 2% of controls, $p < 0.01$), and decreased white matter volume (33% in patients, 5% of controls, $p < 0.001$). When compared to non-carriers, 16p11.2 deletion patients showed an increased frequency of skull base malformations characterized by platybasia, posterior angulation of the dens and crowding of the posterior fossa (41% of patients, 2.5% of controls, $p < 0.001$) and an increased frequency of cerebellar tonsillar ectopia (28% of patients, 5% of controls, $p < 0.001$). These skull base malformations can lead to Chiari I malformations and syringomyelia. Trending toward significance is the comparison of small pituitary size between deletion carriers and non-carriers (17% of deletions, 2.6% of controls, uncorrected $p = 0.028$). The deletions and duplications each separately thus present with a different subset of significant changes in brain development in comparison to non-carriers, highlighting the differences between these two genomic syndromes. Work is ongoing to correlate

these anatomical phenotypes with functional imaging data, cognitive, behavioral and other clinical findings.

Conclusions: This is the first study of its depth of clinical characterization and sample size to systematically identify brain imaging abnormalities in a cohort of genetically defined individuals with susceptibility to autism. There is a significant incidence of pituitary abnormalities and skull base abnormalities in the deletion patients that have clear clinical consequences including presence of Chiari I malformations. Our ongoing work to link cognitive data and functional imaging data with these anatomical changes will likely provide important additional insights into correlates between neuroanatomy and behavior.

115.046 46 Longitudinal Brain Volume Growth Curves in Autism Spectrum Disorder Ages 3 to 25 Years. N. Lange^{*1}, B. G. Travers², B. A. Zielinski³, J. A. Nielsen³, M. Prigge³, A. L. Froehlich³, T. Abildskov⁴, E. D. Bigler⁴, A. L. Alexander⁵ and J. E. Lainhart³, (1)McLean Hospital, (2)Waisman Center University of Wisconsin-Madison, (3)University of Utah, (4)Brigham Young University, (5)University of Wisconsin

Background: Autism spectrum disorder (ASD) is a brain-based, individually heterochronous and heterogeneous developmental disorder, and a lifelong problem. Although brain growth in young children with ASD has been investigated, very little is known about how the brains of these individuals grow and mature as they pass from childhood through adolescence into adulthood.

Objectives: To identify longitudinal brain growth differences between individuals with ASD and healthy age-matched individuals during key developmental epochs, and to further investigate individual heterogeneity.

Methods: Participants included 67 males with ASD aged 3.9-24.4 years and 36 healthy males aged 6.4-25.0 years, each contributing 1-3 MRI scans at 3T over 8 years (272 scans). Repeated volumes of the entire brain, whole-brain gray matter (GM), whole-brain white matter (WM), lobar GM, lobar WM, subcortical GM, lateral ventricles, brainstem and cerebellum were examined by mixed-effects growth curve analysis.

Results: All comparisons are to healthy controls and on average. Reported growth and curvature

percentages represent linear and quadratic growth curve changes. **Total brain volume.** The brains of individuals with ASD had **~14.0% less volume** ($p=0.043$) **yet grew ~1.9% more rapidly at ~3.1%** per year ($p=0.038$), and greater inverted-U shaped decreases during young adulthood (curvature -0.11% versus -0.04 , $p=0.028$). All subsequent differences reported here have been adjusted for total brain volume. **Brainstem.** Subjects with ASD had equal brainstem volume that increased at $\sim 3.0\%$ per year ($p<0.0005$), and greater inverted-U shaped decreases during young adulthood (curvature -0.08% versus -0.06 , $p=0.019$). **Frontal GM.** Subjects with ASD had **~9.8% less frontal GM volume** ($p=0.005$) that increased $\sim 0.1\%$ per year, compared to a decline of 1.2% per year ($p=0.003$). **Parietal lobe.** Subjects with ASD had **~7.0% more parietal lobe volume** ($p=0.033$) that declined $\sim 0.9\%$ more rapidly at $\sim 1.2\%$ per year, with U-shaped increases during young adulthood (curvature $\sim 0.02\%$, $p=0.048$). **Occipital lobe.** Subjects with ASD had **~13.4% more occipital lobe volume** ($p=0.009$) that declined at $\sim 1.2\%$ per year ($p=0.017$). Occipital GM and occipital WM volumes increased equally until young adulthood, during which there were GM increases and WM decreases (curvatures 0.06 and -0.04 , $p=0.001$, 0.033). Temporal lobe, subcortical GM, lateral ventricle and cerebellum volumes were unaffected. No differences in total or regional hemispheric asymmetries were found. After average growth curves were extracted, **subjects with ASD showed more individual volumetric variability** than seen in healthy brain development.

Conclusions: In this investigation, the brains of individuals with ASD grew, and matured, in very different ways compared to the brains of healthy individuals. On average, the ASD sample had less frontal GM volume, which did not decline as in the control sample, and more parietal and occipital volumes that declined more rapidly. During young adulthood, further volumetric decreases in total brain and brainstem volumes, and further increases in parietal lobe volume, were seen in those with ASD. This study also found greater developmental heterogeneity in the brains of individuals with ASD beyond that captured by these average group trends. The relation of these

new findings to the core cognitive and behavioral deficits in ASD is not yet known.

115.047 47 Diffusion Tensor Imaging and Volumetry of Autistic Children in India. Z. A. Assis*¹, S. Srinath², J. Saini², A. K. Gupta², P. R. Naidu³, R. D. Bharath² and U. Rao², (1)*SHRI SATHYA SAI INSTITUTE OF HIGHER MEDICAL SCIENCES*, (2)*NIMHANS*, (3)*N/A*

Background: Childhood autism is now widely viewed as having a developmental neurobiological origin. Hence localised structural and functional brain correlates have to be established. There is no major study discerning the structural and connectivity changes in the autistic children of Indian origin yet in the literature to the best of our knowledge.

Objectives: To study the Diffusion tensor imaging (DTI) findings and compare the brain volumetry in autistic children (diagnosed as per DSM-IV criteria) as compared to age and sex matched typically developed controls.

Methods: Study was conducted at NIMHANS, Bangalore, INDIA. After obtaining ethical approval, a study population of 19 subjects (mean age of 8.79 ± 3.84 years; M: F=16:3) and 34 healthy controls (mean age of 12.38 ± 3.76 years; M: F= 34:0) were imaged by a 3 Tesla MRI scanner using standard protocols. DTI data analysis was carried out using FMRIB Software Library tools version 4.1.6 to create FA maps. Tract based spatial statistics (TBSS) analysis of the Fractional anisotropy (FA) maps was performed using voxel by voxel permutation. Cortical reconstruction and volumetric segmentation (FSL) analysis was performed with the Freesurfer image analysis suite.

Results: We found significantly reduced FA in bilateral corticospinal tracts, corpus callosum, left inferior longitudinal fasciculus, bilateral thalami, nucleus accumbens, left uncinate fasciculus and bilateral optic tracts. Significantly reduced volumes were found in the left accumbens, left pallidum, right thalamus, left hippocampus and bilateral cerebral white matter, after adjusting for age and intracranial volumes.

Conclusions: Our prospective study in a small population of children with ASD under 20 years of age demonstrated significant abnormalities in

various white matter tracts by TBSS analysis of DTI data as well as a few areas of significant volume reduction by FSL analysis as compared to the typically developed healthy controls. We found reduced FA and increased Radial diffusivity (RD) in many of the white matter tracts, with little effect on the Axial diffusivity (AD), suggestive of myelination defects rather than axonopathy. We also found some common areas with both reduced FA and reduced volumes, involving left nucleus accumbens and right thalamus. These data may open gateways for further research to be channelized towards these deep gray matter structures.

115.048 48 White Matter Connectivity Predicts Autism Spectrum Disorder Symptom Severity in High-Functioning Young Adults. C. R. Gibbard*¹, J. Ren¹, K. K. Seunarine¹, J. D. Clayden¹, D. H. Skuse² and C. A. Clark¹, (1)*UCL Institute of Child Health*, (2)*Institute of Child Health, UCL*

Background: Increasing evidence suggests that autism spectrum disorder (ASD) occurs at the extreme of a distribution of social and communication abilities. Diffusion tensor imaging (DTI) studies have shown white matter (WM) abnormalities in tracts involved in social processing in ASD. However, little is known about the relationship between these WM anomalies and the range of behavioural phenotypes observed in ASD and the neurotypical population. Further, the majority of DTI studies in ASD have focussed on children and adolescents. Little is therefore known if the reported WM abnormalities persist into adulthood.

Objectives: We investigated WM microstructure and its relationship to ASD symptom severity across both ASD adults and neurotypical controls using tract-based spatial statistics (TBSS), a whole-brain voxel-based approach. TBSS mitigates registration and smoothing effects found in alternative techniques and enables investigation of the whole WM without prior hypotheses of regions of interest.

Methods: 25 high-functioning ASD (mean age 24.5yr) and 25 neurotypical subjects (mean age 23.22yr) underwent whole-brain T1-weighted (1mm isotropic) and diffusion-weighted (2.5mm isotropic; 60 directions at $b=1000s/mm^2$; 3 interleaved $b=0s/mm^2$) MRI on a 1.5T Siemens Avanto scanner. The diffusion data were pre-processed using FSL, including eddy current

correction and brain-extraction. Subsequently, voxel-wise WM analysis was performed using TBSS that co-registers all diffusion data and generates an average WM skeleton on which statistical comparisons are made. The values for each DTI metric were also averaged across the WM skeleton and correlated with the autism quotient (AQ), a self-reported measure of autistic symptoms. Age, gender, full-scale IQ and whole brain volume were added as nuisance covariates in all analyses.

Results: Voxel-wise analysis of the WM skeleton using TBSS showed widespread regions of significantly reduced fractional anisotropy (FA) and significantly increased mean diffusivity (MD) and radial diffusivity (RD) in ASD compared to controls. Across the whole study population, FA averaged across the WM skeleton was negatively correlated with AQ score ($\rho=-0.38$; $p=0.007$) in ASD, whilst AQ was positively correlated with MD ($\rho=0.46$; $p=0.0009$) and RD ($\rho=0.46$; $p=0.0008$). These correlations were predominately localized in the left hemisphere. Correlations between DTI parameters and subdivisions of the AQ score were strongest for social, communication and attention switching domains and weakest for attention to detail and imagination.

Conclusions: Our finding of very widespread reductions in FA and increases in MD and RD in ASD compared to neurotypical controls suggests that WM microstructural changes in ASD adults are more widely distributed than previously reported. The correlations between WM anomalies and the severity of ASD traits across the whole study population indicate that WM microstructural aberrations form a distribution which is strongly related to a spectrum of abnormal social behaviours, of which ASD is at the extreme. The specific relationships between DTI parameters and sub-divisions of the AQ score suggest that the distributed structural-functional relationship is strongest for social communication ASD traits. Our finding of a separation of IQ from the relationship between WM microstructure and ASD severity is evidence for distinction of core cognitive abilities from the social difficulties central to ASD.

115.049 49 Functional and Structural Connectivity of Frontostriatal Circuitry in ASD. S. Delmonte*¹, J. H. Balsters¹, E.

Background:

Frontostriatal circuitry subserves goal-directed action, playing a key role in emotion, motivation, cognition and the control of movement. Abnormal function and/or connectivity of this circuit may underlie deficits in social interaction and communication, restricted interests and repetitive behaviours and/or other cognitive deficits in ASD. However, few studies have examined connectivity within this circuit in ASD and no previous study has examined both functional and structural connectivity within the same population.

Objectives:

To examine frontostriatal functional connectivity in ASD and to use diffusion tensor imaging (DTI) to investigate associated differences in structural connectivity.

Methods:

28 right-handed male participants with high functioning ASD and 27 right-handed male, age and IQ matched controls took part in the MRI study (Mean age: ASD=17.28 (SD= 3.57); Control=17.15 (SD= 3.64); Mean IQ ASD= 109.25 (SD= 15.04); Control=111.85 (SD= 12.32)). 21 ASD and control participants were retained for the fMRI analysis and 22 ASD and 24 control participants were included in the DTI analysis after excluding subjects for factors such as excessive motion (movements >3mm) and poor data quality. fMRI preprocessing was carried out in SPM8 and functional connectivity analysis was carried out using the CONN toolbox. Seed regions for the functional connectivity analysis were defined within the left and right frontal cortex. Target regions included the left and right striatum (caudate, putamen, accumbens). All ROIs were generated using the Harvard-Oxford probabilistic atlas. DTI preprocessing and analysis was carried out using Explore DTI. Tractography analysis was carried out between the frontal cortex and striatal regions that showed significant differences in functional connectivity, and was confined to intra-hemispheric tracts (i.e. right frontal cortex to right accumbens and right caudate). Fractional Anisotropy (FA), Mean

Diffusivity (MD), Radial Diffusivity (RD) and Axial Diffusivity (AD) were extracted for each tract of interest. T-tests and Mann-Mann-Whitney tests were carried out to examine group differences in functional and structural connectivity respectively. Results were corrected for multiple comparisons using an FDR correction ($p < .05$).

Results:

The ASD group showed increased functional connectivity between the right anterior cingulate and right accumbens/left caudate, the right middle frontal gyrus and right accumbens/right caudate, the right paracingulate gyrus and right accumbens /right caudate and the left paracingulate gyrus and the right accumbens/right caudate. There were no regions that showed significantly reduced connectivity between the frontal cortex and the striatum. Although tracts were reliably constructed for each subject there were no group differences in structural connectivity (FA, MD, RD, AD) in the tracts of interest.

Conclusions:

Results are in keeping with previously reported increased corticostriatal functional connectivity among children with ASD and indicate that increased frontostriatal connectivity persists among adolescents and young adults with ASD. Increased connectivity was recorded in cognitive and limbic (but not sensorimotor circuits) suggesting that abnormal frontostriatal connectivity may be implicated in social and cognitive deficits in ASD. There were no differences in structural connectivity as measured by DTI, suggesting that functional connectivity measures may be more sensitive to differences in connectivity among older subjects with high functioning ASD.

115.050 50 Developmental Differences in the Uncinate Fasciculus Vary by Sex in Autism Spectrum Disorders. S. C. Huang, G. J. Pauley, T. L. Richards, N. M. Corrigan, D. W. Shaw, A. A. Artru, A. Estes, S. Dager and N. M. Kleinmans*, *University of Washington*

Background: Although autism spectrum disorders (ASD) are typically life-long, the symptoms observed in early childhood may improve for some children over the course of development. Our

previous study demonstrated that white matter integrity appears to change from adolescence to adulthood. The major biological change in adolescence is the onset of puberty, which results from an elevation of sex steroid hormones. Since the sex steroid hormones also influence brain structural development, we theorize that the observed brain changes may stem, in part from an interaction between sexual and developmental processes that occur over time both in the brain and in the behavioral expression of ASD.

Objectives: We employed Diffusion Tensor Imaging (DTI) with a probabilistic tracking algorithm to identify white matter tracts in a sample that varied in terms of age, diagnosis, and sex. We hypothesized that (1) there was an interaction between sex and age in white matter integrity in ASD, and (2) the integrity of white matter tracts were related to clinical measures of autism symptoms.

Methods: Forty-seven participants with ASD and 49 with typical development (TD) participated in the study. The ASD group included 27 adolescents (females=5; mean age=14.79±0.75; range=13.58–16.47) and 20 adults (females=6; mean age=24.82±4.63; range=19.43–35.72). The TD and ASD groups were age- and gender-matched. All ASD participants met DSM-IV, Autism Diagnostic Interview-Revised (ADI-R), and Autism Diagnostic Observation Schedule (ADOS) criteria for an ASD. DTI scans were collected on a 3T Philips Achieva MR system (version 1.5, Philips Medical Systems, Best, Netherlands). DTI parameters: single-shot echo-planar sequence (TR/TE/flip angle: 10.5s/63ms/90°, matrix size of 128×128, FoV of 240×240, 2mm slice thickness, 72 slices) with 32 gradient directions and a *b*-factor of 1000s/mm². Probabilistic tractography maps of the uncinate fasciculus (UF), cingulum (CIN), genu (GEN) and splenium (SPL) of corpus callosum were reconstructed with FSL. The mean values of diffusion parameters (FA, MD, AxD, RaD) of each tract were computed. Three-way (age×group×sex) ANOVA was performed on all the diffusion parameters of each tract to test the interaction. Partial correlations were performed between diffusion parameters and clinical measures (ADI-R, ADOS) with full scale IQ as a covariate.

Results: Three-way interactions of sex, age, and diagnosis were found in FA, MD, RaD in the UF ($p=0.023, 0.015, 0.009$) and AxD in SPL ($p=0.007$). Numerous correlations between white matter integrity and ADI-R and ADOS measures were also found. Notably, different correlation patterns were found between males and females with ASD.

Conclusions: This study demonstrated that differences in white matter integrity between the ASD and TD groups varied from adolescence to adulthood and between males and females. The results implied atypical developmental trajectories of white matter tracts in ASD. Further, our correlational analyses indicated that the integrity of different white matter tracts correlated to functional differences and, in some cases, were sex-specific. Our results implied that the pathological developmental trajectory of the UF, a white matter tract associated with socioemotional processing, differs according to sex in ASD. Additional studies with larger numbers of females are needed to confirm these preliminary findings.

115.051 51 Connectivity and Network Efficiency in ASD. J. D. Lewis^{*1}, R. J. Theilmann², J. Townsend² and A. C. Evans³,
(1)Montreal Neurological Institute, McGill University,
(2)University of California, San Diego, (3)McGill University

Background: There is now a consensus that in autism spectrum disorder (ASD) there is reduced long-distance connectivity (Just et al 2007). The status of short-distance connectivity in ASD is less clear. It has been hypothesized that long-distance under-connectivity is matched with an increase in short-distance connectivity (Belmonte et al 2004), but there is a paucity of evidence to support that speculation. Further, there is a lack of understanding of how abnormalities in connectivity interact with each other within the overall network.

Objectives: We investigate connectivity in ASD, for all sets of cortico-cortical connections, and the structure and efficiency of the overall networks, to determine whether altered connectivity in long- and short-distance connectivity are compensatory at the network level.

Methods: T1-weighted (t1w) and diffusion-weighted (dw) scans were collected from 22 male adults with ASD (34.14 ± 10.67 years) and 22 male controls (31.68 ± 8.75 years). CIVET, a fully

automated structural image analysis pipeline, was used to construct white-matter surfaces for each subject, and to segment subcortical regions (Collins et al 1995, Kim et al 2005). Seed masks, stop masks, and target masks were then constructed for use with FSL's *probtrackx*. Seed masks were white-matter; stop masks were the boundary of white-matter; and target masks were the white-matter surface. The dw scans were corrected for distortions using fieldmaps, and affine registered to the t1w volumes using FSL's *flirt*. The dw volumes were then preprocessed with FSL's *bedpostx*, and probabilistic tractography was seeded from 10000 random locations within each voxel of the seed masks; once to generate the number of tracts connecting voxels in the target mask, and a second time to generate the length of those connections. The AAL atlas was then overlaid on the target masks, and the connectivity between cortical regions calculated, as well as the mean length of those connections. Measures of local, global, and small-world efficiency, as defined by Latora and Marchiori (2001, 2003), were computed for each subject, and group differences in efficiency were assessed, as well as group differences in connectivity between all pairs of AAL regions.

Results: Group comparisons of connectivity for all pairs of AAL regions showed a mix of under- and over-connectivity in ASD, but predominately under-connectivity, both in long- and short-distance connections. The ASD group showed strongly reduced local efficiency, which was broadly distributed, an increase in global efficiency, and a non-significant reduction in small-world efficiency.

Conclusions: Connectivity abnormalities in ASD represent a shift from an organization with strong local connectivity and sufficient long-distance connectivity to support efficient communication between these local modules, to an organization which compensates for reduced long-distance connectivity by sacrificing local structure. This is not a shift toward greater short-distance connectivity, but rather toward a randomly connected network.

115.052 52 Concordance of White Matter and GREY Matter Abnormalities in Autism Spectrum Disorders. F. Bianco^{*1}, F. Cauda², T. Costa², S. Palermo³, M. Diano², S. Duca², G. Geminiani³ and R. Keller¹, (1)ADULT AUTISM CENTER,

ASL TO2, TURIN, ITALY, (2)CCS FMRI, KOELLIKER HOSPITAL, TURIN, ITALY, (3)DEPARTMENT OF PSYCHOLOGY, UNIVERSITY OF TURIN, TURIN, ITALY

Background:

Over the last decade, the application of neuroimaging techniques has played an important role in increasing knowledge about structural brain organization in ASD compared to normal development. Voxel-based morphometry (VBM), a computational based technique that measures focal differences in concentrations of brain tissue, has provided new insights into the changes in brain structures associated with ASD. Various clues suggest that related neural areas may vary mutually, with morphometric changes in the same or reverse direction, due to reciprocally trophic effects mediated by direct axonal connections.

Objectives:

We inspected two fundamental unanswered questions in the literature on Autism Spectrum Disorders (ASD): i) Are abnormalities in white (WM) and grey matter (GM) consistent with one another? And ii) Are WM morphometric alterations consistent with alterations in the GM of areas connected by these abnormal WM bundles and vice versa? The aim of this study is to bridge this gap.

Methods:

After selecting voxel-based morphometry and diffusion tensor imaging studies comparing autistic and normally developing groups of subjects, we conducted an Activation Likelihood Estimation (ALE) meta-analysis to estimate consistent brain alterations in ASD. Multidimensional scaling was employed to test the similarity of the results. The ALE maps were then analyzed to identify the areas of concordance between GM and WM areas.

Results:

We found statistically significant topological relationships between GM and WM abnormalities in ASD. The most numerous were negative concordances, found bilaterally but with a higher prevalence in the right hemisphere. Positive

concordances were found in the left hemisphere. Discordances reflected the spatial distribution of negative concordances. Thus, a different hemispheric contribution emerged, possibly related to pathogenetic factors affecting the right hemisphere during early developmental stages. Besides, WM fiber tracts linking the brain structures involved in social cognition showed abnormalities, and most of them had a negative concordance with the connected GM areas. We interpreted the results in terms of altered brain networks, and their role in the pervasive symptoms dramatically impairing communication and social skills in ASD patients.

Conclusions:

These results represent a new step in focusing the biological basis of the core symptoms of ASD that we have described as an altered network balance, with a different hemispheric representation, interestingly possibly related to different hemispheric development timing. A pathogenetic factor activating a genetic input could alter the balance of brain development, also involving epigenetics, possibly mediated by an inflammatory and endocrinological mechanism and widely disrupting brain connectivity, thus reflecting the pervasive symptoms dramatically damaging quality communication and social skills in the early development of ASD patients.

115.053 53 Children with SLOS Demonstrate a Different Pattern Brain Microstructure Than Autism and Rett Syndrome. R. W. Lee*¹, A. Diaz-Stransky², E. S. Jung¹, A. Thurm³ and F. D. Porter⁴, (1)*Kennedy Krieger Institute*, (2)*Johns Hopkins University School of Medicine*, (3)*National Institute of Mental Health*, (4)*National Institute of Child Health and Human Development*

Background: Smith-Lemli-Opitz Syndrome (SLOS) is an autosomal recessive disorder of cholesterol biosynthesis that results in multiple congenital malformations, intellectual disability and autistic behavior. Diffusion tensor imaging (DTI) studies in children with autism show increased mean fractional anisotropy (mFA) in infancy, followed by a decrease in mFA between ages 2.5 to 9 years, when compared with typically developing (TD) controls. A similar pattern has been described in individuals with Rett syndrome. There are no published DTI studies in SLOS.

Objectives: The following study aims to compare the DTI findings in SLOS with TD controls. Outcome measures include mFA, MD, and volume for 40 atlas-based ROI previously described in studies of individuals with autism and Rett syndrome. A secondary aim is to compare the DTI findings in SLOS with those reported in autism and Rett syndrome.

Methods: Ten children (mean= 10.1 years +/- 5.5) with SLOS, and 27 TD controls (mean=9.7 years +/-7.5) received 3T MRI scans. Statistical analyses applied student's T-test. SLOS children underwent ASD testing with ADI-R and ADOS by expert clinicians who emitted a clinical judgment using DSM-IV criteria.

Results: Individuals with SLOS showed higher mFA, decreased volume, and decreased MD compared to controls for the majority of ROI studied (30/40, 75%). These results contrast with the pattern of microstructural findings in children with autism and Rett syndrome. Pending analysis within SLOS group will compare microstructural diffusion characteristics between autistic and non-autistic SLOS children.

Conclusions: The pattern of DTI findings in SLOS differ from those reported in autism, Rett syndrome and controls. These findings suggest that while autistic symptoms are present in these three neurodevelopmental disorders, a unique microstructural substrate in SLOS may be underlying the autistic behaviors described in the phenotype. Further studies are required to reveal the neurobiologic causes of autistic behavior in SLOS.

115.054 54 Insular Volume Reduction Is a Common Feature Between Adolescents with High-Functioning Autism and First Episodes of Psychosis. M. Parellada*¹, L. Pina-Camacho² and J. Janssen³, (1)*Instituto de Investigación Sanitaria Gregorio Marañón, IiSGM. Hospital General Universitario Gregorio Marañón, CIBERSAM, Madrid, SPAIN*, (2)*Instituto de Investigación Sanitaria Gregorio Marañón, IiSGM. Hospital General Universitario Gregorio Marañón, CIBERSAM*, (3)*Imaging Laboratory*

Background: Data from neurocognitive and genetic studies show common features and risk factors between autism spectrum disorders (ASD) and psychosis. Social cognition is a domain of abnormal performance in which both ASD and psychosis patients fail. There is very little data

available on brain structural abnormalities common to the two groups of disorders.

Objectives: To study areas of shared brain structural abnormalities related to the social brain network.

Methods: In this study, we MRI scanned 34 adolescents with high-functioning ASD (HF-ASD), 36 with a first episode of psychosis (FEP), and 34 healthy controls. We compared volumes, cortical thickness, and surface area of *a priori* selected regions of interest associated with social cognition (amygdala, insula, pars opercularis, superior temporal region, and precuneus region). The effect of IQ in the studied regions was also acknowledged via correlating IQ with the dependent variables and using it as a covariate variable when appropriate.

Results: HF-ASD and FEP patients had smaller insular volumes than normal controls [mean difference in left insula: HF-ASD vs. controls 4.37 cc ($p=0.036$), psychosis vs. controls 6.39 cc, $p=0.006$; right insula: HF-ASD vs. controls 5.03 cc ($p=0.006$), psychosis vs. controls 5.19 cc, $p=0.021$), after correcting for intracranial volume and age. Mean precuneus volume was smaller in both patient groups, reaching statistical significance in the case of HF-ASD, compared with control subjects ($p=0.035$ and $p=0.01$ for left and right precuneus, respectively).

Conclusions: This study shows that the insula (considered an important multimodal area involved in high-order mental processes) and, to a lesser extent, the precuneus region (important for self-awareness, episodic memory, and social and other communication) are areas of abnormal structure common to psychosis and HF-ASD patients. Further studies are needed to determine whether these areas of common abnormality are specific to these disorders or are shared with other human mental disorders.

115.055 55 White Matter Abnormalities in HF-ASD and Their Unaffected Siblings, A Diffusion Tensor Imaging Study. R. Calvo Escalona^{*1}, M. Rosa², A. Calvo Boixet³, O. Puig Navarro¹ and L. Lázaro García², (1)CIBERSAM, (2)Hospital Clinic of Barcelona, (3)IDIBAPS

Background:

The Diffusion Tensor Imaging (DTI) is an innovative technique that reports several data of white matter (WM) integrity, analyzing different indexes as a Fractional Anisotropy (FA), Mean Diffusivity (MD), Radial Diffusivity (RD) and Axial Diffusivity (AD). Previous studies found reduced FA and increased MD and RD in several areas of WM in ASD children, as the anterior thalamic radiation (ATR), the corpus callosum, the uncinate fasciculus, the corticospinal tract, the internal capsule, the pedunculi cerebri, the inferior longitudinal fasciculus, the inferior fronto-occipital fasciculus, the superior longitudinal fasciculus and the cingulum (Brito, 2009; Cheon, 2011; Ameis, 2011; Shukla, 2011). Barnea-Goraly (2010) also reported aberrancies of WM in healthy siblings of ASD children, but their findings have been not replicated in similar samples.

Objectives:

The aim of the present study is to analyze the nature of WM structural connectivity in high functioning ASD (HF-ASD) patients and in their unaffected siblings.

Methods:

Subjects: Participants were 35 HF-ASD children and adolescents (mean age=12.31, SD=3.10; 31 male, 4 girl), 18 healthy comparison (HC) controls (mean age=11.53, SD=3.07; 17 male, 1 girl) and 17 ASD siblings (mean age=14.07, SD=4.75; 9 male, 8 girl). There were differences in sex, IQ and socioeconomic status (SES) within groups, but these variables were included as additional covariates. All patients fulfilled ASD criteria on DSM-IV and ASD diagnosis were confirmed with the ADI-R. Inclusion criteria included an IQ > 70 in all participants.

Procedures: DTI maps were acquired using 3 Tesla Siemens MAGNETOM TIM Trio by employing a DTI sequence using echo planar imaging (EPI) pulse sequence with diffusion-weighted (acquisition plane: sagittal, TR:9300ms, TE:94ms, b:1000s/mm, n of diffusion gradients:30, slice thickness:2mm, voxel size:2x2x2mm³). FA, MD, L1 and RD maps were generated using FSL. Diffusion images were corrected for eddy current distortion, corrected for motion and registered to 3D T1 using FLIRT. New segmentation of GM and

WM were employed to calculate the flow fields using DARTEL that were applied to DTI maps to normalize to MNI space, smooth (4 mm Gaussian kernel) and Voxel Base Analysis was done using SPM8. Intracranial volume, age, gender, SES and IQ were used as covariates, and statistical threshold criteria was set at $p < 0.05$ corrected for multiple comparison FWE (Family Wise Error correction) at cluster level.

Results:

Compared to controls, HF-ASD participants showed decreased FA in the left ATR (MNI space coordinates (mm)=[-16 -26 10], $p(\text{FWE})=0.012$ cluster-level and cluster size=83). These coordinates were quoted in JHU White-Matter Tractography Atlas using FSL (FMRIB Software Library, Oxford, UK). In ASD siblings, we found increased MD values in the left area that involves the ATR, the cingulum, the forceps major, the inferior fronto-occipital fasciculus and the inferior and superior longitudinal fasciculus (MNI space coordinates (mm)=[-26 -54 6], $p(\text{FWE})=0.000$ cluster-level and cluster size=148). There were no significant differences in WM structure between the ASD and siblings groups.

Conclusions:

Our finding of similar abnormalities of WM in ASD children and their unaffected siblings, could contribute to the investigation of the meaning of WM alterations in the families of children with ASD.

115.056 56 Functional Connectivity MRI Lateralization in Autism Spectrum Disorder. J. A. Nielsen^{*1}, J. S. Anderson¹, M. A. Ferguson², A. L. Froehlich¹, J. R. Cooperrider¹, A. Cariello³, P. T. Fletcher¹, B. A. Zielinski¹, E. D. Bigler¹, A. L. Alexander⁴ and J. E. Lainhart¹, (1)University of Utah, (2)University of Utah School of Medicine, (3)Utah Autism Research Project, (4)University of Wisconsin

Background: A left- and right-lateralized functional network is characteristic of typical development (Liu *et al.* 2009; Nielsen *et al.* 2012). Classical language regions and regions of the default mode network make up the left-lateralized functional network, whereas regions involved in attention make up the right-lateralized functional network. Abnormal lateralization of functional activity in autism has been reported, however, it

is unclear whether abnormal functional lateralization is restricted to classical language regions or if it diffusely affects one or both lateralized functional networks.

Objectives: To determine whether abnormal functional lateralization in autism occurs focally in specific regions of interest or diffusely across lateralized functional networks.

Methods: The preprocessing of 964 (447 autism scans and 517 typically developing control scans) resting-state functional MRI scans from the **Autism Brain Imaging Data Exchange** (http://fcon_1000.projects.nitrc.org/indi/abide/index.html) followed standard image processing procedures. Using an independent analysis done on 1,019 typically developing controls, 9 regions involved in the left-lateralized functional network and 10 regions involved in the right-lateralized functional network were identified as the regions involved in the most lateralized connections (Nielsen *et al.* 2012). A functional lateralization index (fLI) was calculated for each of the 81 pairwise connections (36 pairwise connections between the 9 left-lateralized regions and 45 pairwise connections between the 10 right-lateralized regions) for each subject by subtracting the connection strength (determined by correlating the BOLD time series between two regions and taking hyperbolic arctangent of the correlation coefficient) in the right hemisphere from the connection strength in the left hemisphere. Group comparisons were made on the fLIs for the 81 connections using two-sample t-tests with a Bonferroni correction. The correlation between fLI and the following behavioral measures was also investigated: autism severity (as measured by the ADOS social + communication scores), handedness, and age.

Results: Two connections in the left-lateralized network—Wernicke’s area to the posterior cingulate cortex (PCC) and Wernicke’s area to the temporoparietal junction (TPJ)—demonstrate a lack of left lateralization in the autism group compared to the typically developing group (Wern-PCC: $t = 3.36$, $p = 0.0008$; Wern-TPJ: $t = 3.30$, $p = 0.001$). The connection between Wernicke’s area and the PCC negatively correlates with autism severity ($r = -0.13$, $p = 0.02$).

Conclusions: Abnormal lateralization of functional connectivity during rest in autism is restricted to specific left-lateralized connections rather than diffusely affecting either the left- or right-lateralized functional networks. Also, as left lateralization increases between Wernicke's area and the posterior cingulate cortex, autism severity decreases.

References: Liu, H, *et al.* *Evidence from intrinsic activity that asymmetry of the human brain is controlled by multiple factors.* (2009) PNAS, vol. 106, no. 48, pp. 20499–20503.

Nielsen, JA, *et al.* *Left and Right Dominant Functional Connectivity Networks.* (2012, June). Poster presented at the Organization for Human Brain Mapping's 18th Annual Meeting, Beijing, China.

115.057 57 Evidence for Selective Damage to Cognitive Cortico-Cerebellar Circuits in Autism Spectrum Disorder. J. H. Balsters*¹, S. Delmonte¹, N. Wenderoth² and L. Gallagher¹, (1)Trinity College Dublin, (2)ETH Zurich

Background:

A growing body of literature suggests that the cerebellum contributes to a wide variety of behaviours, both cognitive and motor. This is largely supported by anatomical evidence from both humans and non-human primates which shows that specific cerebellar lobules are exclusively interconnected with either motor regions (cerebellar lobules HV, HVI, HVIIb, HVIII) or prefrontal and parietal cortices (cerebellar lobules Crus I/II). Cerebellar deficits are routinely found in Autism Spectrum Disorder (ASD), but the functional and behavioural consequences of this are not yet clear. Given that theories of cerebellar function are largely based on its extrinsic connectivity, investigating the differences in functional connectivity within these circuits should help us better understand how cortico-cerebellar deficits contribute to ASD pathology.

Objectives:

This study uses resting state fMRI to investigate cortico-cerebellar connectivity changes in ASD.

Methods:

28 right-handed, medication free, male participants with high functioning ASD and 27 right-handed male, age and IQ matched controls participated (Mean age: ASD=17.28 (SD= 3.57); Control=17.15 (SD= 3.64); Mean IQ ASD= 109.25 (SD= 15.04); Control=111.85 (SD= 12.32)). 21 ASD and control participants were retained for the fMRI analyses after excluding subjects for factors such as excessive motion (movements >3mm) and poor data quality. fMRI preprocessing was carried out in SPM8 and functional connectivity analysis was carried out using the CONN toolbox (ROI->Voxel). The cerebellar atlas of Diedrichsen *et al* (2009) was used to extract timecourses (principle eigenvariate) for each cerebellar lobule. Age and IQ were modeled as regressors of no interest. Results were corrected for multiple comparisons using FDR correction ($p < 0.05$).

Results:

It has been repeatedly shown that cerebellar lobules Crus I and II are interconnected with prefrontal and parietal regions. Our analyses showed that connectivity between Crus II and prefrontal/parietal cortices (specifically bilateral intraparietal sulcus and right middle frontal gyrus) was reduced in ASD compared to controls. We also found connectivity between left Crus I and the vermal lobule IX was reduced in ASD. These two cerebellar regions have been shown to be functionally interconnected using clustering algorithms, and additionally interconnected with prefrontal/parietal cortices (Bernard *et al* 2012). Finally we found that there was greater connectivity between the right putamen and right lobules I-IV in ASD compared to controls.

Conclusions:

The cortico-cerebellar system is known to contribute to both cognitive and motor control, however these results suggest that it is specifically the cognitive cortico-cerebellar circuits that are altered in ASD. It is likely that decreased connectivity of the prefrontal/parietal cortico-cerebellar loop contributes to cognitive deficits in ASD, potentially working memory which has been shown to activate these regions (Stoodley *et al* 2012). Given that motor cortico-cerebellar circuits do not differ between groups it is unlikely that cortico-cerebellar connectivity is related to motor

deficits seen in ASD such as repetitive behaviors (although these may still be caused by other cerebellar abnormalities). Further analyses of neuropsychological data are necessary in order to better relate these differences in cortico-cerebellar connectivity to differences in ASD symptomology.

115.058 58 Reduced Amygdala Volumes in Adolescents with Autism Spectrum Disorders Parallels Negative Autistic Trait-Amygdala Correlations in Typically Developing Adolescent Males. G. Wallace*¹, B. Robustelli¹, N. Dankner¹, L. Kenworthy², J. Giedd¹ and A. Martin¹, (1)*National Institute of Mental Health*, (2)*Children's National Medical Center*

Background: Previous neuroimaging studies implicate the amygdala as key in the aberrant neural circuitry underlying the social-emotional difficulties experienced by individuals with autism spectrum disorders (ASD). Abnormal amygdala volumes in ASD have been consistently shown in prior investigations; however, whether there is an amygdala enlargement or reduction is dependent on the age of participants. In ASD, generally greater amygdala volumes are reported among young children while adolescents and young adults may exhibit reduced amygdala size. Nevertheless, this amygdala volume reduction during adolescence and young adulthood remains an open question. Furthermore, it is unclear whether there are subclinical links between normal variation in amygdala volumes and autistic traits among typically developing individuals. Such a relationship would link the full variability in ASD behavior with the amygdala, as has been done with cortical structures, most prominently superior temporal sulcus (Wallace et al., 2012).

Objectives: The purpose of the current study is to compare amygdala volumes in adolescent and young adult males with ASD versus matched typically developing (TD) males and to assess the link between amygdala volumes and self-rated autistic traits in the TD group.

Methods: 41 males with ASD (diagnosed using DSM-IV criteria and the ADI/ADOS) and 40 TD males provided high-resolution 3 Tesla anatomic magnetic resonance imaging scans. Groups were matched on age (ASD mean=16.75 +/- 2.84; TD mean=17.04 +/- 2.73) and IQ (ASD mean=113.27 +/- 15.09; TD mean=114.03 +/- 10.74). The FreeSurfer image analysis suite (version 5.1) was used to derive lateralized volumes for the amygdala. Self-ratings of autistic

traits were obtained within the TD group using the Autism Spectrum Quotient (AQ).

Results: The amygdala was found to be significantly smaller in adolescent males with ASD as compared to TD males ($F=5.18$, $p<.05$), which became a trend effect after controlling for intracranial volume, age, and IQ ($F=3.16$, $p=.08$). This group difference was particularly strong for the right amygdala ($F=6.12$, $p<.05$), even after covarying the effects of these nuisance variables ($F=4.11$, $p<.05$). Paralleling this group difference; as self-ratings of autistic traits increased, amygdala size decreased ($r=-.55$, $p<.01$) in the TD group, and this association held after partialling intracranial volume, age, and IQ ($pr=-.41$, $p<.05$). This correlation was found on both the left ($r=-.55$, $p<.01$) and right ($r=-.46$, $p<.01$) sides, though after covariation of the nuisance variables, only the left side remained significant ($pr=.42$, $p<.05$), while the right side dropped to trend levels ($pr=-.31$, $p=.08$).

Conclusions: The present study showed that amygdala volumes are indeed reduced among adolescents and young adults with ASD (in contrast to the reported enlargement during early childhood). Extending the literature, we found that as self-ratings of autistic traits increased, amygdala volumes decreased in the TD group. This pattern is similar to prior cortical (thickness) findings of other key 'social brain' structures (e.g., superior temporal sulcus) in TD populations (Wallace et al., 2012). By showing both ASD group reductions in amygdala volumes and negative correlations between subclinical ASD behavior and amygdala size in the TD group, these findings further implicate the amygdala in the pathophysiology of ASD.

115.059 59 DTI in the Cerebral Cortex Correlates with Axon Bundle Organisation: Investigation of Regional Differences in Autism. R. McKavanagh*, M. Jenkinson, C. Emin, K. Miller and S. Chance, *University of Oxford*

Background: Recently there has been increasing interest in applying DTI to the cortex, particularly looking at the primary diffusion direction and how it varies across the cortex. However, to date the structural correlates of this anisotropic diffusion in the cortex have not been examined quantitatively. Therefore, this study looked at the relationship between measures of cortical anisotropy and

histological measurements of the radial columnar organisation of the cortex.

Objectives: To determine the relationship between cortical anisotropy and organisation of axonal bundles and to investigate brain regional differences in autism.

Methods: Structural and DTI scans were collected post-mortem from 6 ASD brains, 4 control brains and 9 multiple sclerosis brains (a neurological comparison group). The scanning was carried out using a protocol specifically devised for fixed post-mortem tissue as described in Miller et al (2011). Radial cortical anisotropy was analysed using the novel CHIPS software. Following scanning, samples from several regions were removed and sectioned. Sections were either Nissl stained to enable minicolumn measurements to be taken (described in Chance et al (2008)), or stained with Sudan Black to enable measurements of axonal bundles. Image analysis software was used to measure the centre-to-centre spacing of the axon bundles and the cell minicolumns, and the width of the myelinated bundles themselves.

Results: We found a strong correlation between our measures of radial anisotropy in the cortex and several histological measures of the radial columnar structure. In particular, the measurements of the myelinated bundles showed a good correlation with measures of radial diffusion in the cortex. In addition we found that cortical anisotropy reflects the regional variation in the cortex detected in the histological data.

Conclusions: The present work provides important information on the structural correlates of the observable cortical anisotropy in high-resolution DTI scans and provides validation of the CHIPS technique for investigating cortical correlates of neurological and psychological disorders. Future work to develop this technique for in-vivo use would allow for longitudinal studies of cortical development and alteration in disorders such as autism.

115.060 60 Compared to What? Early Brain Overgrowth in Autism and the Perils of Population Norms. A. Raznahan^{*1}, G. L. Wallace¹, L. Antezena¹, A. Thurm¹, D. Greenstein¹, R. Lenroot², S. J. Spence³, M. Gozzi¹, A. Martin¹, S. E. Swedo¹ and J. Giedd¹, (1)*National Institute of Mental Health*,

(2)*University of New South Wales*, (3)*Children's Hospital Boston*

Background:

The presence of a robust association between Autism Spectrum Disorder(ASD) and early brain overgrowth(EBO) is widely accepted, and continues to influence the cutting edge of ASD research. The bulk of published data regarding early brain growth in ASD comes from studies of head circumference(HC), an excellent proxy for brain size in early childhood.

Objectives:

To reappraise of the evidence base for EBO in ASD given recent reports that several large independent samples of typically developing children show EBO relative to HC reference norms used by several seminal EBO reports in ASD.

Methods:

We systematically review all published HC tests of the EBO hypothesis in ASD (34 studies encompassing ~ 3k ASD and 60k controls participants), and analyze new data from a cohort of 57 preschool-aged male Caucasian children (35 ASD, 22 healthy controls) with ~ 330 longitudinal HC measures between birth and age 18 months. Throughout, we test if the strength of evidence for EBO depends on the type of control data with which HC data in ASD are compared. We supplement traditional sources of HC norms in ASD research (e.g CDC) with recently published "Primary Care Norms" (PCNs): the largest (~500k HC measures between birth and 18 months) contemporary set of US-based HC norms.

Results:

Systematic Review -- Eighty-five percent of all HC studies in ASD make use of HC norms. Cross-sectional studies that do not find evidence for brain enlargement in ASD tend to include a comparison with controls rather than solely relying on HC norms ($p=0.0006$). Longitudinal HC studies that compare ASD data to CDC norms unanimously identify rapid HC centile increases in ASD between birth and ~age 12 months. In contrast, most longitudinal studies comparing HC

growth between ASD participants and controls do not find evidence for EBO in ASD during the first year of life. By integrating prior reports, we robustly confirm the well-replicated pattern of EBO in ASD relative to CDC norms, but show that the timing of this EBO is mimicked by PCN norms.

New Data -- We did not find any cross-sectional differences in raw HC between ASD and controls at any pediatric surveillance time-point in the first 18 months of life, or group differences in raw HC change between time-points. Both ASD and controls groups showed abnormally accelerated HC growth relative to CDC HC norms, but not PCN norms.

Conclusions:

The best-replicated aspect of EBO in ASD reflect generalizable HC norm biases rather than a disease-specific biomarker. Removing these biases leaves partial support for a subtle divergence of HC growth between a sub-group of clinically-recruited children with ASD and community-recruited controls during the second year life that (i) results in ~5mm group difference in mean HC at 18 months (~ effect size 0.5d), and (ii) may index body size and SES related confounds. Our findings provide a cautionary reappraisal of the EBO hypothesis in ASD and raise broader concerns about the use of popular growth norms in clinical and academic medicine.

115.061 61 Clustering Multiple Mouse Models Related to Autism Based On Neuroanatomy. J. Ellegood*, R. M. Henkelman and J. P. Lerch, *The Hospital for Sick Children*

Background: Autism Spectrum Disorders (ASDs) are complex and still poorly understood. They are highly heritable, yet no single gene discovered to date accounts for more than 1-2% of known cases (Abrahams and Geschwind, 2010). Currently 250+ genes have been associated with Autism in the human population (gene.sfari.org), and while ASD is associated with communication and social deficits, as well as repetitive behaviours, individual clinical presentations are highly heterogeneous (Reiss, 2009).

Objectives: The purpose of this work is to take an expansive approach in order to identify the similarities and differences in neuroanatomy across the autistic spectrum. To this end, we

examined 20+ mouse models of ASD candidate genes using high resolution structural MRI.

Methods: Mouse models of Autism were acquired from the Jackson Laboratory or through collaboration with other research labs. Ten mice minimum were included for each individual genotype and each model had a corresponding wild type control.

MRI Acquisition - A 7.0 Tesla MRI (Varian Inc., Palo Alto, CA) was used to acquire ex-vivo anatomical images of brains within skulls. A T2-weighted, 3D fast spin-echo sequence was used, with a TR of 2000 ms, and TE_{eff} of 42 ms over 6 echoes, two averages, field-of-view of 14 × 14 × 25 mm³ and matrix size = 250 × 250 × 450 giving an image with 0.056 mm isotropic voxels. Total imaging time was ~12 h.

Individual Data and Cluster Analysis - We used image registration to align the brains from each individual model, which allowed us to calculate the volumes on a regional (62 different regions) (4) or a voxelwise basis (voxel - 3D pixel). Group differences were calculated as effect sizes for each model. Using hierarchical clustering methods, the models were then grouped together based on their similarities and differences.

Results: Across all models the most affected regions were the corpus callosum and the cerebellum. The clustering segregated the models into 4 distinct groupings, 1) the models in which the differences in the autism model were larger compared to the wild type, 2) where they were smaller, 3) where they were unchanged, and 4) where there was some mixture of larger and smaller differences. The Mecp2³⁰⁸ Rett syndrome model was found to be quite similar to the Neuroligin3 R451C knockin model as well as the Intergrinβ3 knockout. The voxelwise changes within the corpus callosum in both the Intergrinβ3 model and the Neuroligin3 R451C model also overlapped significantly. Unexpectedly, despite the well-known connection between the Neuroligins and Neurexins in the brain, the Neurexin1a knockout did not overlap with the Neuroligin3 R451C knockin.

Conclusions: Here we group autism models together based solely on their neuroanatomical

differences. These findings help to explain some of the variability seen in human autism as well as highlight regions of interest, such as the corpus callosum and the cerebellum, that are commonly found in ASD. Importantly, the whole brain analyses performed allow us to group disparate autism mouse models by their phenotypic similarities.

115.063 63 Decreased Cortical Thickness in Autism Spectrum Disorder: A Large-Sample Investigation Using Surface-Based Morphometry. D. Yang, S. K. Mitchell, C. Cordeaux, I. Y. Murphy, K. A. Pelphrey and R. J. Jou*, *Yale University*

Background: Cortical thickness (CT) abnormalities in autism spectrum disorder (ASD) are reported in the current research literature. However, several major limitations exist, including (a) highly mixed results with some studies reporting increased CT in ASD while others reporting decreased CT, (b) heterogeneous methods with some studies using voxel-based morphometry (VBM) leading to less accurate results (because the cerebral cortex is highly folded and curved) relative to surface-based morphometry (SBM), and (c) small sample sizes which may lead to erroneous conclusions.

Objectives: This study addresses the aforementioned limitations by comparing CT using SBM in large samples of individuals with ASD and typically developing (TD) participants.

Methods: There were 213 total participants: 105 children and adolescents with ASD, including 88 males (mean age = 9.7 ± 3.7 years) and 17 females (mean age = 9.3 ± 3.8 years), and 108 TD participants (mean age = 10.37 ± 3.4 years) matched on age, sex, and cognitive functioning. Cognitive functioning was measured by Differential Ability Scales-II (DAS-II). The diagnosis of autism was confirmed with Autism Diagnostic Observation Schedule (ADOS) and Autism Diagnostic Inventory-Revised (ADI-R). T1-weighted, whole-brain structural MRI scans were acquired using a 3-Tesla scanner. The structural MRI scans were processed and analyzed using the FreeSurfer image analysis suite version 5.1.0, which consists of automated tools for reconstruction of the brain from high-resolution MRI data. With some manual correction, the program facilitated accurate and precise CT measurements of 66 different brain regions based on the Desikan-Killiany atlas. These

measurements were entered into the Statistical Package for the Social Sciences (SPSS) version 19, and between-group comparisons of CT were conducted using multivariate analysis of covariance (MANCOVA).

Results: MANCOVA controlling for age, cognitive functioning, and intracranial volume revealed that children and adolescents with ASD had consistently lower CT than TD across several regions known to be involved in processing social information. These regions included the bilateral banks of the superior temporal sulcus (STS) as well as the left superior temporal, middle temporal, entorhinal, and fusiform gyri, and finally the left pars orbitalis and supramarginal gyrus.

Conclusions: By using SBM and a large sample of participants, this study documents specific areas of cortical thinning in ASD confined to regions involved in social information processing. These abnormalities likely have important implications for the social-communication deficits in ASD.

115.064 64 Aberrant Right Temporo-Thalamic Connectivity in ASD an fMRI and Graph Theory Study. A. Nair*¹, C. L. Keown², M. Datko³, A. J. Khan² and R. A. Müller², (1)*SDSU/UCSD Joint Doctoral Program in Clinical Psychology*, (2)*San Diego State University*, (3)*University of California San Diego*

Background: The thalamus is an important subcortical relay structure, through which most sensory information is routed. It plays a crucial role in visual, auditory, and somatosensory functions, as well as attention and motor control. Various lines of evidence have suggested thalamic abnormalities in ASD (e.g., Chugani et al. 1997, Friedman et al. 2003). Highly specific patterns of thalamocortical connectivity have been demonstrated in typically developing (TD) individuals using functional connectivity MRI (fMRI; Zhang et al. 2008, 2010; Fair et al. 2010). In a prior study (Nair et al., under review), this thalamocortical pattern of connectivity was replicated for TD children, whereas children with ASD showed mostly reduced connectivity, accompanied by overconnectivity between right temporal lobe and thalamus. However, this study did not examine thalamic connectivity of specialized regions within the temporal lobe.

Objectives: To investigate which specific functional regions within the right temporal lobe drive temporo-thalamic overconnectivity in ASD.

Methods: Resting-state functional MRI data were acquired for 6:10 minutes on a 3T GE scanner for 30 children and adolescents with ASD (ages 8-17 years) and 35 age, sex, IQ, and motion-matched TD participants. Data were preprocessed using AFNI and included motion and field map correction, spatial smoothing, isolation of low frequency fluctuations ($.01 < f < .1$), and normalization to Talairach space. Freesurfer was used to obtain parcellations for: right temporal pole (rTP), superior temporal gyrus (rSTG), middle temporal gyrus (rMTG), inferior temporal gyrus (rITG), fusiform gyrus (rFG), and parahippocampal gyrus (rPHG). A mask was created from the right thalamic overconnectivity cluster detected in our previous study to extract time series and examine connectivity with the Freesurfer regions. As an alternative approach to quantifying connectivity, graph theory was used to compute the functional density ratio of present connections ($r > .25$) out of all possible ones, between the thalamus and each parcellation of the temporal lobe.

Results: fMRI results showed overconnectivity (ASD > TD; $p < .01$ corr.) between right thalamus and rPHG, rIFG, rMTG, posterior rSTG, and rFG. Conversely, significant underconnectivity (ASD < TD; $p < .05$ corr.) was observed for rTP and anterior rSTG. Graph theory results additionally showed significantly greater functional density connections of rPHG and rITG with the right thalamus in the ASD (compared to the TD) group.

Conclusions: Our findings suggest that right temporo-thalamic overconnectivity in ASD is driven by distributed regions within the thalamus, including medial, inferior, and posterolateral temporal cortices. Anterior portions of the right temporal lobe showed inverse effects (underconnectivity). Further investigations will be needed to determine the functional relevance of this dichotomy, such as potentially compensatory roles of right temporo-thalamic overconnectivity in memory, emotional, auditory, higher visual, or language functions.

Hegarty II^{*1}, B. J. Ferguson², R. M. Zamzow², S. E. Christ¹, M. O. Mazurek¹ and D. Q. Beversdorf¹, (1)University of Missouri, (2)University of Missouri-Columbia

Background:

Current behavioral interventions for autism focus on increasing quality of life and language development whereas pharmacological interventions are directed at managing the secondary manifestations such as anxiety and repetitive and obsessive behaviors. Pharmacological research directed at the core features of autism is limited. Propranolol, a beta-adrenergic antagonist, has been shown to improve verbal problem solving in typically developing controls as well as people with autism, and research into propranolol's pharmacotherapeutic effects is warranted.

Current theories suggest that autism may be due to altered network flexibility within cortical regions important for information processing and findings suggest both hypo- and hyper-activation, depending on the network. Functional magnetic resonance imaging, fMRI, allows for the measurement of a correlate of flexibility of access to networks, as assessed by functional connectivity. We therefore wish to determine fMRI alterations with and without beta-adrenergic agents. We have previously shown the beneficial effects of propranolol during verbal problem solving may be due to increased flexibility of access to cortical networks important for language processing. We wish to extend this line of research to facial and emotional processing and hypothesize that during propranolol administration subjects will show increased connectivity.

Objectives:

Our objective is to examine the mechanism of the beneficial effects of a currently available pharmacotherapeutic agent, propranolol, on the core features of autism by assessing functional connectivity using fMRI during facial and emotional salience processing.

Methods:

We examined a pilot sample of individuals with autism during administration of propranolol,

nadolol, and placebo. Nadolol provides a control for general vascular effects on BOLD fMRI because nadolol is a beta-adrenergic antagonist that does not cross the blood brain barrier. After drug administration, subjects were placed in the 3T magnetic resonance scanner at the University of Missouri Brain Imaging Center and asked to complete a faces-matching task. Stimuli consisted of faces either exhibiting angry, fearful, or neutral expression. *A priori* regions of interest, ROIs, were used to extract region-specific activation in the frontal cortex, fusiform gyrus, middle temporal gyrus, superior temporal gyrus, posterior parietal cortex, and amygdala. Correlations between pairs of ROIs were calculated and transformed using Fishers z calculation.

Results:

The facial matching task activated our main regions of interest, fusiform and amygdala, allowing for the use of these regions as seeds for functional connectivity analyses. We found a significant effect for drug such that functional connectivity was significantly altered during propranolol trials compared to placebo.

Conclusions:

With this preliminary data, we show that the cognitive benefits of propranolol in autism may extend beyond language processing and may be due to alterations of flexibility of access to networks due to effects on beta-adrenergic receptors. Better understanding of the effects of the beta-adrenergic system on neuronal processing, especially in the autism population, and modulation of the beta-adrenergic system pharmacologically could lead to development of additional treatments for the core features of autism. Additional research is required to fully understand these alterations and determine possible biomarkers, such as genetic status, of who may benefit most from beta-adrenergic intervention.

115.066 66 Incidental Findings On Neuroimaging for Asymptomatic Children with Autism Spectrum Disorders. S. E. Levy^{*1}, K. Shekdar², A. N. Browne³, C. M. DeLussey², S. Qasmieh³, P. Prabhakar², T. P. Roberts³ and R. T. Schultz³, (1)*Children's Hospital of Philadelphia/ University of Pennsylvania*, (2)*CHOP*, (3)*Children's Hospital of Philadelphia*

Background: Incidental findings (IF) on head neuroimaging have been frequently reported in adults and children, and more commonly in children with neurologic or neurobehavioral disorders such as autism spectrum disorders (ASD). However, there is little data available about IF in children and adolescents with and without ASD who are asymptomatic and who have agreed to participate in magnetic resonance imaging (MRI) studies.

Objectives: Report the prevalence and describe characteristics of IF in a population of neurologically asymptomatic children with idiopathic ASD and typically developing controls who have volunteered for imaging studies.

Methods: We reviewed consecutive structural head MRI studies of neurologically asymptomatic children (6 – 16 years) , with and without ASD, who consented to participate in ongoing functional MRI (fMRI) studies at the Center for Autism Research (CAR) of The Children's Hospital of Philadelphia between January 3, 2012 and September 30, 2012. All imaging was obtained on a Siemens Verio 3T scanner, with a 32 channel head coil. Studies were reviewed by 1 of 8 board certified neuroradiologists, blinded to case status and without systematic case assignment. Final reports were reviewed by 2 study team authors (blinded to case status) to determine whether IFs required further follow-up.

IFs were divided into categories – BBIF (brain based, such as pineal cyst, ventricular enlargement, others) and NNIF (non-neurologic, such as sinus abnormalities with inflammatory changes, others), and SIF (significant IF, where intervention such as notification of family and primary care provider or other subspecialist was indicated).

Results: Reports of 116 subjects were reviewed, N=76 ASD (92% male, average age 10.0 + 2.3 years), N=40 typically developing controls (TDC) (80% male, average age 10.5 + 3.0).

The prevalence of any IF for ASD was 22% (N=17), with BBIF 12% (N=9) and NNIF 11% (N=8). Less than half (45%, N=4) of BBIF were SIF, and no NNIF were SIF. TDC prevalence of any IF was 40% (N=16); BBIF frequency 25%

(N=10) and NNIF 15% (N=6). The frequency of SIF was BBIF 13%, NNIF 3%. For all SIF the family and primary care provider (PCP) were notified to arrange follow-up.

BBSIF included arachnoid cyst, cerebellar abnormalities (Chiari I malformation, low lying tonsils, cerebellar ectopia), vascular anomaly (hypoplastic right vertebral artery, old perfusion injury, dilation left carotid). NNSIF included intervention for severe sinusitis. Of all the subjects, 6% had SIFs.

Conclusions: We report higher rates of incidental findings than previous studies, which may be related to superior imaging resolution or increased attention to findings. Our sample is a neurologically asymptomatic group of children with ASDs and typical development who volunteered for participation in fMRI studies at CAR. Overall prevalence of incidental findings was 28% (N=33). In subjects with an IF, less than one quarter (7% of all study participants) notification of caregivers was deemed appropriate. This confirms other reports suggesting the need of specific clinical management protocol(s) to assess the significance (and reportability) of incidental findings.

115.067 67 Resting State Functional Network Organization and Topological Properties in Autism Spectrum Disorder. S. E. Christ^{*1}, R. M. Zamzow² and J. D. Johnson¹, (1)University of Missouri, (2)University of Missouri-Columbia

Background: Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by impairments in social communication and restricted, repetitive behaviors. Resting-state functional connectivity MRI (fcMRI) measures subtle correlations in low-frequency blood oxygenation level-dependent (BOLD) signal changes between brain regions while individuals are "at rest" or not otherwise engaged in a directed cognitive task. Whereas findings from past studies suggest that functional connectivity is altered in individuals with ASD as compared to typically developing individuals without ASD, the nature of this aberration has not been clearly delineated.

Objectives: In the present study, we used advanced graph theory methods to examine resting-state fcMRI data from a large sample of individuals with and without ASD in hopes of

gaining additional insight into how the topological properties of brain functional networks differ based on factors such as diagnosis (ASD vs non-ASD) and age.

Methods: Resting state fcMRI data was collected from 28 adolescents and adults with ASD (mean age = 14.9 years) and an age- and gender-matched comparison group of 35 typically developing individuals without ASD (mean age = 15.6 years). Following pre-processing and anatomical parcellation into 90 cortical and subcortical regions of interest (ROIs), functional partial correlation matrices were generated. The matrices for the participants in each group were averaged, thresholded to obtain undirected binary matrices, and then visualized as mean networks. Overall differences in network membership and structure were evaluated. Lastly, topological parameters were calculated to evaluate group differences in both local and global network properties.

Results: The ASD and control group mean networks differed in node membership and organization. Overall, 73 connections comprise the ASD group network whereas the control group network contains 67 connections. The ASD and non-ASD networks were similar in that both were characterized by numerous long-distance connections (both anterior-to-posterior and left-to-right). However, the ASD network was characterized by a higher number of local connections.

Following network visualization, topological parameters were calculated for each participant and compared between groups. The two groups did not differ significantly in global network efficiency, $t(63) = 1.40, p = 0.17$. Local efficiency (i.e., the efficiency with which information is transferred at a local level), however, was greater for the ASD group as compared to the non-ASD group, $t(63) = 1.93, p = 0.05$.

Conclusions: The results of the present study indicate potential alterations in function network organization and topological properties in ASD. Further analysis is needed to fully characterize these differences within the contexts of both age and symptom severity.

115.068 68 Brain Morphometry Abnormalities in Patients with Autism Spectrum Disorders and Schizophrenia: Same or Different?. M. Assaf^{*1}, A. Ahmadi², C. Hyatt², C. A. Berwise² and G. Pearlson¹, (1)*Institute of Living, Hartford Hospital / Yale University*, (2)*Hartford Hospital*

Background: Although autism spectrum disorders (ASD) and schizophrenia (SZ) have distinct clinical symptomatology, recent studies suggest that they may share common deficits in social skills and underlying etiopathology. Recent neuroimaging techniques have demonstrated brain morphometric abnormalities in both SZ and ASD patients, with potential overlaps. More specifically, structural brain studies in ASD patients suggest that as for SZ, abnormal volume and cortical thickness (most likely thinning) might underlie the neuropathology of the disease. Direct comparisons between these two patient groups, however, have not yet been performed to determine which brain regions have common versus distinctive structural abnormalities.

Objectives: The major goal of this pilot study was to study the brain structure in both SZ and ASD patients in comparison to matched healthy controls (HC) to explore structural abnormalities, commonalities and differences in brain structure in SZ and ASD. We hypothesized that while SZ and ASD will demonstrate unique deficits they will also share some abnormalities.

Methods: In this study we analyzed the morphometric parameters of structural MRI (sMRI) data (MPRAGE sequence) collected at the Olin Center from 14 high-functioning ASDs (Autistic disorder, Asperger's syndrome and PDD-NOS), 19 chronic SZ patients (schizoaffective patients were excluded) and 19 HC, ages 15 to 30, with normal range IQ (>80). Groups were matched on sex, race, full-scale IQ and handedness. Structural data were analyzed using FreeSurfer tools (version 5.1, <http://surfer.nmr.harvard.edu>) to measure local gyrification index (LGI).

Results: For LGI, one-way ANOVA demonstrated a main effect of group in left inferior frontal gyrus (IFG), superior temporal gyrus (STG) and sulcus (STS) and inferior parietal lobule (IPL), as well as lingual and fusiform gyri; and in right inferior temporal sulcus (ITS) (significant following Monte Carlo simulation at a cluster-wise probability of

$p < 0.05$ FWE). Follow-up *t*-tests demonstrated that for left IFG both SZ and ASD groups showed reduced LGI compared to HC. Group-specific LGI abnormalities were seen in right ITS and left STS/IPL and fusiform gyrus, where only SZ showed lower LGI, compared to HC and ASD.

Conclusions: In this pilot study we directly compared brain morphometry of ASD and SZ patients to HC and found reduced cortical gyrification in IFG in both patient groups. Conversely, parietal and temporal regions showed diagnosis-specific abnormalities in cortical gyrification. Importantly, all implicated regions are known to be involved in cognitive processes related to social functioning and language, domains that are deficient in both SZ and ASD. Implications for patients' diagnosis and symptoms will be discussed.

115.069 69 Neuroanatomical Basis of Autism in Girls. K. Supekar^{*}, L. Uddin and V. Menon, *Stanford University*

Background:

Autism spectrum disorder (ASD) is diagnosed in females less often than males by a factor of 1 to 4. Emerging behavioral accounts suggest that females are rated to be less severely autistic than males on several measures of early social development. Remarkably, to date, there have been no systematic attempts to characterize potential brain structural differences underlying the distinct behavioral profiles observed in females and males with ASD. Such work is critical for understanding the etiology of this heterogeneous disorder, as well as for understanding why the prevalence is low in females.

Objectives:

To characterize and compare brain structure in girls and boys with ASD.

Methods:

Behavioral and structural MRI data from 25 7-13y old girls with ASD (mean age: 10.3y, mean IQ: 103), and 25 IQ-matched boys with ASD (mean age: 10.3y, mean IQ: 102) was obtained from Autism Brain Imaging Data Exchange (ABIDE) – a

public repository of behavioral and neuroimaging data.

Brain morphometry was assessed using the optimized voxel-based morphometry method. Structural images were resliced and spatially normalized to the stereotactic space. The normalized images were then segmented into gray matter (GM), white matter, and cerebrospinal fluid compartments. The GM images were modulated and smoothed. Group differences in GM volume were examined by comparing modulated smoothed GM images of girls with ASD with those of boys with ASD, using state-of-the-art multivariate pattern analysis (MVPA).

Results:

Females and males did not differ in overall severity of childhood autism. There were also no sex differences in social and communication deficits. However, females showed less severe restricted and repetitive behavior ($p < 0.01$).

To delineate neural markers that underlie the unique behavioral profile in female children with ASD, we compared brain structure in ASD girls with ASD boys. Using MVPA analysis, we found that GM in several cortical regions could discriminate female and male children with ASD. Notably, GM volume in the precentral gyrus, fusiform gyrus, angular gyrus, cerebellum, and the insula showed high accuracies (85-90%) for distinguishing girls from boys. Additionally, we found that the GM volume in the precentral gyrus and cerebellum was correlated with scores on the Repetitive/Restrictive Domain of the ADI-R ($p < 0.001$) such that the female children with the least impairment in the Repetitive/Restrictive domain showed greatest GM volume in regions involved in motor function. No such relationship was observed in boys.

Conclusions:

Our findings not only provide evidence for distinct behavioral profiles in girls with ASD, compared to boys, but also show a link between these behavioral differences to brain structural differences demonstrating for the first time that at earlier ages closer to disorder onset, the brain in female children with ASD is structured in ways

that may contribute to reduced behavioral impairments. These findings may reflect different developmental trajectories between females and males with ASD. More generally, brain-based gender-specific biomarkers of ASD developed here may eventually be used to aid in early and more accurate detection of the heterogeneous disorder in females, as well as targeted intervention strategies.

115.070 70 Short Range Over-Connectivity and Long Range Under-Connectivity in the Resting State Network in Autism Spectrum Disorders. K. A. R. Doyle-Thomas^{*1}, W. Lee², N. E. Foster³, A. Tryfon³, T. Ouimet⁴, K. L. Hyde⁵, A. C. Evans³, L. Zwaigenbaum⁶, E. Anagnostou⁷ and .. NeuroDevNet ASD Imaging Group⁸, (1)*Bloorview Research Institute*, (2)*Hospital for Sick Children*, (3)*McGill University*, (4)*Montreal Children's Hospital Research Institute*, (5)*Montreal Neurological Institute, McGill University*, (6)*University of Alberta*, (7)*Holland Bloorview Kids Rehabilitation Hospital*, (8)<http://www.neurodevnet.ca/research/asd>

Background: There is converging evidence of atypical functional brain connectivity within task specific and idle neural networks in individuals with Autism Spectrum Disorders (ASD). It has been reported that individuals with ASD have greater short to medium range connections and fewer long range connections. However, previous studies have been small in size and/ or have not been carried out in children and young adolescents with ASD.

Objectives: We examined (1) functional connectivity among regions of the resting state network [i.e. precuneus (central hub) with anterior cingulate cortex, and middle temporal gyrus] and (2) functional connectivity between the precuneus and neighbouring regions [i.e. posterior cingulate cortex, calcarine, cuneal, lingual gyri and the primary visual cortex].

Methods: We report here on data from 65 participants between the ages of 9-15 years (ASD: $n=31$, and typically developing controls: $n=34$). A significant between-group difference was found in IQ (ASD: 93.14 ± 18.2 and TD: 116.61 ± 9.07 , $p < 0.05$). Functional Magnetic Resonance Imaging data were pre-processed using a combination of AFNI, FSL and locally developed software tools. Each participant's functional scan was coregistered to their anatomical scan, and ROIs were drawn using the Harvard-Oxford cortical atlas. ROIs were

iteratively eroded until the mean intravoxel cross-correlation within an ROI reached a threshold of 0.8 (based on the methods of Golestani and Goodyear, 2011). For each participant, we calculated the coefficient of determination (R^2 , or the square of the correlation coefficient) among all regions, bilaterally. We tested for significant mean differences between control and ASD subjects using a two-tailed t-test.

Results: Significantly higher correlations were found between the precuneus and neighbouring regions in ASD compared to controls (all $p < 0.05$) and higher connectivity in the resting state network was observed in controls compared to individuals with ASD (all $p < 0.05$).

Conclusions: These preliminary results suggest short range over-connectivity in children and adolescents with ASD, in the context of a under-connected resting state network. These findings extend our current knowledge of atypical functional connectivity in ASD into a younger population.

115.071 71 A Spectrum of Cortical Surface Complexity in Autism, Dyslexia, and Controls As Measured by Spherical Harmonics. E. L. Williams^{*1}, B. A. Dombroski², M. Nitzken¹, A. S. El-Baz¹, A. E. Switala¹ and M. F. Casanova¹, (1)*University of Louisville*, (2)*University of Louisville School of Medicine*

Background: In many aspects of cortical development, autism and dyslexia occupy opposing extremes of a neuroanatomical distribution. Autism exhibits increased density of neocortical minicolumns, increased gyrification, decreased gyral window size, reduced corpus callosal volume, and enhanced radiate white matter volume; dyslexia, in contrast, exhibits increased minicolumnar density, reduced gyrification, greater gyral window size, and increased corpus callosal volume. Both conditions are typified by neurogenic anomalies and heterogeneous ectopic clusters, pinpointing early cortical development in their respective etiologies. While gyral complexity has previously been estimated using various gyrification indices, Spherical Harmonics (SH) offers the researcher a greater precision in recapitulating the shape of a 3-D form such as the brain, lending itself well to the study of gyral complexity in autism and dyslexia.

Objectives: Based upon previous evidence, we have utilized SH, a set of basic functions defined on the unit sphere, to measure cerebral surface complexity in autistics, dyslexics, and controls to determine overall levels of complexity and divergence between groups.

Methods: Raw data for our measurements of overall surface complexity utilizing spherical harmonics comprised T1-weighted MRI of the brains of 8 individuals, 1 of them female, with autism (8 y–38 y of age, mean 24 y); 13 dyslexic men (18.5 y–40.5 y of age, mean 30 y); and 431 controls, 224 female, comprising our normative data (4.7 y–22.3 y of age, mean 12 y). Triangular mesh representations of the cerebral cortical surface in scanner-based, RAS coordinate system were mapped to the unit sphere using an attraction-repulsion algorithm. Mesh topology was preserved, so that the transformed meshes triangulated the sphere. This mapping defined three scalar functions on the sphere: $R(\theta, \phi)$, $A(\theta, \phi)$, and $S(\theta, \phi)$, each of which was represented as an SH series. Truncating the series at a particular maximum degree L_{max} provides an approximation to the cortical surface that incorporates greater detail as L_{max} is increased. We computed a shape index, s , for each surface by summing the truncation error as L_{max} ranged from 1 to 80, inclusive. Measurements for cellular analysis of individual gyri were taken from our previous postmortem studies.

Results: As predicted by our theoretical model, the shape index varied significantly by diagnostic category. Autism exhibited a greater level of surface complexity, dyslexia presented within the lower ranges of our three groups, while controls occupied the median ranges.

Conclusions: When utilizing SH to measure overall surface complexity of the brain, autism and dyslexia display two extremes of a single distribution, while controls occupy an intermediate range between the two. Autism and dyslexia occupy similar diametric positions when measuring other aspects of corticalization. Together, this evidence supports our theory of a cerebral spectrum, one in which autism and dyslexia illustrate its two phenotypic extremes.

115.072 72 Gray Matter Network Property Differences in Children with Autism Spectrum Disorder. N. E. Foster^{*1}, K. A. R.

Doyle-Thomas², A. Tryfon³, T. Ouimet³, A. C. Evans³, E. Anagnostou², L. Zwaigenbaum⁴, K. L. Hyde¹ and .. NeuroDevNet ASD Imaging Group⁵, (1)McGill University, (2)Holland Bloorview Kids Rehabilitation Hospital, (3)Montreal Neurological Institute, (4)University of Alberta, (5)<http://www.neurodevnet.ca/research/asd>

Background: Structural brain imaging studies have revealed differences between individuals with autism spectrum disorders (ASD) and Typical Development (TD), particularly in frontal brain regions. Functional connectivity studies have shown differences in correlated activity and functional network properties in ASD. However, there are relatively few investigations on detailed measures of grey matter comparing ASD and TD children, and no one has examined structural brain connectivity using graph theoretical network analysis applied to cortical thickness measures in ASD.

Objectives: To examine structural brain connectivity as measured by regional correlations in cortical thickness (CT) across the brain in ASD versus TD.

Methods: We present preliminary data from 30 ASD and 36 TD control children as part of the 'NeuroDevNet ASD project', an ongoing multi-site study on brain and behavioral development in ASD. Ethical approval was granted by the Montreal Neurological Institute Research Ethics Board. The groups were matched on age (from 6-16 years old), and all subjects had an IQ above 70 (except 2 ASD individuals). Vertex-wise CT values were generated from T1 structural MR images using the CIVET pipeline. Correlations of mean CT among 74 cortical regions were calculated separately for the ASD and TD groups, and then tested for differences while controlling the false discovery rate. Cortical connectivity analyses were conducted on the thresholded correlation matrix in order to calculate binary network graphs, as well as network global and local efficiency measures separately in ASD and TD.

Results: Examination of interregional correlations revealed greater connectivity in the ASD group in frontal, parietal and temporal lobes. Increased connectivity was mostly within hemispheres. Diminished connectivity in ASD was found in frontal, parietal and temporal lobes, and mostly

between hemispheres. In comparing overall network connectivity using graph theory, we found significantly enhanced local efficiency in the ASD brain, combined with a trend toward diminished global efficiency.

Conclusions: We provide novel evidence for atypical structural brain connectivity in ASD children using graph theoretical network analyses of cortical thickness. These results are consistent with the idea that short-range connectivity is often enhanced, and long-range connectivity diminished, in ASD.

115.073 73 Longitudinal Age-Related Changes in Cortical Thickness From Childhood to Adulthood in Autism. M. D. Prigge^{*1}, J. A. Nielsen¹, E. D. Bigler¹, T. Abildskov², A. L. Froehlich¹, A. L. Alexander³, N. Lange⁴, B. A. Zielinski¹ and J. E. Lainhart¹, (1)University of Utah, (2)Brigham Young University, (3)University of Wisconsin, (4)McLean Hospital

Background: Cortical development across the lifespan in autism is unknown. Greater age-related decrease in cortical thickness in the occipital and temporal lobes were reported in a preliminary longitudinal investigation by Hardan and colleagues (2009) in adolescent males (aged 8-12 years at baseline) scanned twice over 30 months. We aim to expand on these findings.

Objectives: To describe longitudinal age-related changes from childhood to adulthood in cortical thickness in individuals with autism compared to typical development.

Methods: Freesurfer derived cortical thickness measurements (<https://surfer.nmr.mgh.harvard.edu/ftp/articles/desikan06-parcellation.pdf>) were examined in 98 males with autism (age range 3-36 years at first scan) and 61 typically developing males (age range 4-39 years at first scan). Each participant was scanned 1-3 times, on average every 2.5 years, on a Siemens 3T MRI scanner (total of 353 scans). Mixed effects models were used to describe longitudinal cortical thickness growth in the autism group in comparison to typical development.

Results: Age-related decreases in cortical thickness were found across the entire cortex in both autism and typical development. Significantly greater age-related cortical thinning

was found in autism bilaterally in the occipital cortex (cuneus, lateral occipital, lingual, pericalcarine) and the majority of the parietal regions (left supramarginal, right precuneus, bilateral inferior and superior parietal and postcentral gyrus). In the frontal lobe, greater age-related cortical thinning in autism was found in the left frontal pole, precentral gyrus, pars triangularis, rostral middle frontal, right paracentral, and bilateral pars opercularis.

Significant group by age interactions were found in only two temporal lobe regions. The left bank of the superior temporal sulcus and right transverse temporal gyrus showed greater thinning with age in autism. There were no group differences in longitudinal thickness changes in cingulate cortex.

The only region with significant group differences in mean cortical thickness was the left rostral middle frontal cortex, which was 2.8% thicker in autism ($p=0.01$; at centered age of 14.75 years).

Conclusions: This study is the first to describe longitudinal age-related cortical thickness changes in autism from childhood into adulthood. In the absence of group mean differences for most regions (at centered age of 14.75 years), developmental differences were apparent and greater age-related cortical thinning was found in autism. The occipital and parietal lobes were most affected, but group differences in age-related changes in subregions of the frontal and temporal lobes also emerged. Future analyses will examine potential clinical correlates for individual differences in atypical age-related trajectories.

115.074 74 Neuroanatomical Differences Between ASD Patients and Controls in the Abide Cohort. R. Toro^{*1}, R. Delorme², F. Amsellem², G. Huguet¹ and T. Bourgeron³, (1)*Institut Pasteur*, (2)*Hôpital Robert Debré*, (3)*Paris Diderot University*

Background: The aetiology of Autism spectrum disorders (ASD) appears to be very heterogeneous. In addition to an environmental component, recent studies suggest that hundreds of different genetic mutations may also trigger an ASD phenotype. On the other hand, the central nervous system shows a remarkable plasticity and robustness, and is in many cases capable of compensating important perturbations. The possibility of studying large populations is then critical if we aim at distinguishing the subtle pathological traces that may differentiate the ASD

neuroanatomy from the huge neuroanatomical diversity characteristic of humans.

Objectives: We have analysed various neuroanatomical parameters in a large, multicentric, freely available, cohort of high-functioning ASD patients (N=525) and matched controls (N=560) – the ABIDE project. Our objective was to characterise the neuroanatomical variability in the ASD group within the context of normal neuroanatomical diversity.

Methods: We used validated automatic segmentation tools (Afni, FSL, FreeSurfer, and our own software) to obtain measurements of intracranial volume, brain volume, total grey and white volume, lobar volumes, volumes of different subcortical structures as well as cortical surface reconstructions of the pial surface and the white/grey matter interface. The original datasets and the results of the automatic analyses were visually quality controlled. All measurements were log-transformed and we used a general-linear model to account for the confounding effects of age, sex and scanning centre. We performed univariate comparisons of the differences in mean values between cases and controls, and used F-tests to compare differences in dispersion. We are currently using multivariate analyses to study the pattern of variability between cases and controls, as well as analyses of allometric scaling for regional volume, cortical surface extension, gyrification and thickness.

Results: Our first analyses do not reveal significant differences in mean volume of the different structures, however, we observed a statistically significant larger dispersion within the ASD group compared with controls.

Conclusions: The availability of large open databases is a major step forward in the study of the structure and function of the brain of patients with ASD. Being able to study this large cohort will allow the community to have a common ground to test different methodological approaches and validate previous results obtained in smaller case/control groups. We performed an extensive neuroanatomical analysis of the ABIDE cohort, which we plan to make open to the community. Our results did not show the larger incidence of macrocephaly or total brain volume observed in previous studies, however, we

observed a statistically significant larger variability. This larger variability may be the sign of a system failing to compensate a too important perturbation during development. Further analyses, including multivariate analyses of the patterns of neuroanatomical variability, should allow us to better characterise these finding.

115.075 75 Regional Differences in Gray Matter Structure in Children with Autism Spectrum Disorder. N. E. Foster*¹, K. A. R. Doyle-Thomas², A. Tryfon¹, T. Ouimet¹, A. C. Evans¹, E. Anagnostou², L. Zwaigenbaum³, K. L. Hyde⁴ and .. NeuroDevNet ASD Imaging Group⁵, (1)Montreal Neurological Institute, (2)Holland Bloorview Kids Rehabilitation Hospital, (3)University of Alberta, (4)McGill University, (5)<http://www.neurodevnet.ca/research/asd>

Background: Structural brain imaging studies have revealed differences between individuals with autism spectrum disorders (ASD) and Typical Development (TD), particularly in frontal brain regions. However, there are few detailed studies of gray matter structural differences between ASD and TD children using multiple structural imaging techniques.

Objectives: To better document gray matter structural differences in ASD versus TD children using multiple structural brain imaging measures, including cortical thickness (CT), Voxel Based Morphometry (VBM) and Surface Area (SA).

Methods: We present preliminary data from 30 ASD and 36 TD control children as part of the 'NeuroDevNet ASD project', an ongoing multi-site study on brain and behavioral development in ASD. Ethical approval was granted by the Montreal Neurological Institute Research Ethics Board. The groups were matched on age (from 6-16 years old), and all subjects had an IQ above 70 (except 2 ASD individuals). CT, gray matter VBM, and SA data were generated from T1 structural MR images using the CIVET pipeline. The general linear model was used to test for group differences in CT, VBM and SA, covarying for age and scanner site.

Results: The CT group comparison revealed greater CT in ASD in left and right frontal regions including middle frontal gyrus and medial orbitofrontal gyrus. The VBM analysis revealed increases in gray matter density in the same brain regions. Combined increases in CT and SA in ASD were found in fusiform gyrus. Increased SA was

also found in left superior temporal gyrus, adjacent to primary auditory cortex.

Conclusions: We provide convergent evidence through multiple structural imaging techniques for regional differences in gray matter in ASD children. Structural differences found in frontal and temporal cortex correspond to previous functional differences found in ASD in regions known to be involved in core features (e.g., atypical social cognition and communication), and atypical sensory perception in ASD.

Services Program

116 Adults, Lifespan, Methods

116.076 76 A Longitudinal Examination of Change in Vocational Outcomes for Adults with ASD. J. L. Taylor*¹ and M. M. Seltzer², (1)Vanderbilt Kennedy Center, (2)Waisman Center, University of Wisconsin-Madison

Background:

The transition from adolescence to adulthood is a time of amplified risk for individuals with ASD. It is unknown, however, whether problems in employment and educational attainment in the years immediately after high school exit represent "momentary perturbations" in development or a "turning point" in development with long-lasting effects throughout adulthood.

Objectives:

The present study addressed this question by examining 10-year trajectories of vocational outcomes for adults with ASD, as well as the personal characteristics and environmental resources that predicted outcomes.

Methods:

Participants were 161 adults with ASD (ages 18-52 at the start of the study, M=30.9 years) who were part of a larger longitudinal study, and who had all exited high school prior to the start of the study. Approximately three-fourths (72%) of the sample was male and 80.7% had an intellectual disability (ID). Data were collected at 6 time points over a 10-year period. Vocational Outcomes were measured at each time using the Vocational Index (Taylor & Seltzer, 2012). This index is composed of nine ordered categories,

ranked on a scale from 1 to 9; ordering of categories reflects the independence necessary to achieve a vocational/educational activity, as well as whether the adult participated in activities for more than a minimal amount of time.

Independent variables included indicators of personal characteristics (ID; sex; autism symptoms; maladaptive behaviors; independence in activities of daily living) and environmental resources (family income; number of services; unmet service needs; maternal support).

Results:

Multi-level models were used to examine whether personal characteristics and environmental resources were related to 1) concurrent Vocational Index scores (Time 1 scores); 2) Vocational Index scores measured 10 years later (Time 6 scores); and 3) change in Vocational Index scores over time (slope).

Overall, Vocational Index scores were declining over the 10-year study period, $B = -.04$, $p < .05$, with less than one-quarter of the sample (24%) evidencing any improvement. Greater declines were observed for females relative to males, $B = -.09$, $p < .05$. On average, Vocational Index scores of females with ASD declined over 1 full point on the 9-point scale; this decline was 4 times greater than what was observed for males. Personal characteristics of the adult with ASD predicted higher Vocational Index scores at Time 1 and Time 6, including no comorbid ID ($Bs = 1.55$ and 1.10 for Time 1 and Time 6, respectively, $ps < .01$), more independence in activities of daily living ($Bs = .06$ and $.06$ for Time 1 and Time 6, respectively, $ps < .05$), fewer maladaptive behaviors ($B = -.04$, $p < .05$ for Time 6), and fewer autism symptoms ($B = -.11$, $p < .05$ for Time 6). Environmental resources were not related to Vocational Index scores.

Conclusions:

On average, adults with ASD were losing ground in their vocational and educational activities over the 10-year study period – particularly females. Discussion will focus on the role of sex, independence in activities of daily living, and behavior problems in the vocational activities of these adults.

116.077 77 Longitudinal Outcomes in Autism: Community Inclusion and Living Skills in Adulthood. K. M. Gray*¹, C. Keating¹, J. R. Taffe¹, A. V. Brereton¹, S. L. Einfeld² and B. J. Tonge¹,
(1)Monash University, (2)University of Sydney

Background: The overwhelming majority of studies indicate that adults with autism remain largely dependent upon others for support in day to day activities. Beyond age and cognitive ability, little is known about childhood characteristics and how they relate to adult outcomes.

Objectives: This study aimed to describe adult community inclusion (living arrangements, daytime activities, community social involvement) and living skills (community, self care, and communication skills) outcomes in a community sample of children and adolescents with autism. We also aimed to examine childhood predictors of outcomes including the role of childhood individual (age, gender, IQ, behaviour and emotional problems) factors and the environment (socio-economic disadvantage).

Methods: This study followed a cohort of 119 children and adolescents over 18 years with five waves of data collection. The mean age of the sample at Time 1 was 8.7 years, and 24.8 years at Time 5. Participation has been consistently high throughout the study, with 77% of the original sample participating at Time 5. Outcomes in terms of community inclusion were assessed for all participants at Time 5, encompassing information on living arrangements, daytime activities, and community social involvement. Living skills were assessed using the Index of Social Competence.

Results: A significant proportion (61%) of participants remained living in the family home at the time of adult follow up (Time 5). Degree of ID was the only significant predictor of Time 5 living arrangement being 'in care' or 'independent', and the only significant predictor of Time 5 main daytime activity being study or paid employment. Childhood (Time 1) behaviour and emotional problems were not associated with Time 5 daytime activities, living arrangements, or living skills. Higher rates of childhood behaviour problems did indicate a higher likelihood of being engaged in activities for fewer than 20 hours per week. Community social involvement in

adulthood (Time 5) was not significantly associated with Time 1 age, gender, degree of ID, socio-economic disadvantage, or behaviour and emotional problems. Self care and communication skills were associated with Time 1 socio-economic disadvantage. The relationship between childhood behaviour problems and Time 5 living skills was found to be significant across the three domains of living skills.

Conclusions: Compared to earlier research, fewer adults with autism are now living in care and more are engaged in daytime activities. Despite this, a significant number continue to live at home with their families and the number in paid employment is still low. Poor living skills are associated with these outcomes, and research needs to address the best way to improve skills to facilitate and support community inclusion. Childhood degree of ID is consistently associated with adult outcomes, and children with severe ID seem to be particularly at risk for poor community inclusion outcomes as adults. It is however important to consider that childhood IQ is not the sole predictor of outcome, and a better IQ does not guarantee a better outcome. Most adults with autism continue to need support from families and services.

116.078 78 ASD in the Hospital: Making It Easier for Children, Families, and Staff. J. Miller*¹, T. P. Gabrielsen¹, K. A. Bouser², J. Zelli³, K. Hart-Livingston³, M. N. Davignon³ and E. Friedlaender³, (1)*Center for Autism Research*, (2)*The Children's Hospital of Philadelphia*, (3)*Children's Hospital of Philadelphia*

Background: Given the rising prevalence of ASD, health care systems are challenged to safely and expertly interface with this growing patient community. Unfortunately, many characteristics of ASD can interfere with the efficient and effective delivery of almost all aspects of health care. From routine health care encounters to more highly specialized evaluations and interventions within a hospital-based setting, individuals with ASD can become easily overwhelmed and distressed during a health care encounter. This can make providing health care difficult for the patient, family, and staff, and over time make it less likely that individuals with ASD will receive or seek necessary medical treatments. Health care systems and individual providers of medical services are largely unprepared to adapt to the needs of these

individuals, and need training on alternative technologies, adapted instruments, and accommodations within standard practice.

Objectives: This presentation will outline how we have worked to translate the model of Positive Behavioral Support, used successfully within education and treatment settings for individuals with autism, to an acute medical setting in order to predict and prevent problem behaviors that challenge delivery of safe, quality care. We will introduce a series of strategies tailored to address how to identify patients who may need special assistance, how to prepare children with ASD and their families in advance of a hospital visit, and how to help providers organize and structure a patient encounter.

Methods: Suggested interventions include: identifying patients who may need special accommodations through the electronic medical record, priority scheduling to reduce wait times, room assignment to quieter areas, developing materials to create visual schedules within patient care locations, recommendations for environmental modifications to patient care areas; tools to improve accuracy of pain assessment, discrete modifications to bedside care, and methods to more successfully share information among providers and with families. Direct training of staff on characteristics of ASD and the use of targeted interventions to adapt standard practice is also necessary.

Results: Targeted interventions can facilitate staff communication and improve the interaction with individuals with ASD, which will in turn lead to more successful health care encounters. Better understanding of how children with ASD experience and communicate about pain will help health care providers make more accurate assessments of pain, which will also increase the quality of care.

Conclusions: It is critical to consider how we provide health care to individuals with ASD. We found it possible to replicate a PBS model of intervention within an acute medical setting that is easily self-sustaining at low cost, and generalizable to different health care settings. Training staff on how ASD can impact a health care visit and how to make accommodations within standard practice can empower hospital

staff to provide an excellent patient experience to individuals with ASD and their families.

116.079 79 Facilitators and Barriers to Care of Children with Autism Spectrum Disorders Undergoing Procedures. M. N. Davignon*, E. Friedlaender and S. E. Levy, *Children's Hospital of Philadelphia*

Background: Children with Autism Spectrum Disorders (ASDs) are frequently seen in medical settings for common childhood illnesses and injuries as well as chronic conditions associated with ASDs. Characteristics associated with ASDs make medical encounters more challenging. Common behavioral strategies used with typical children often fail in this population, and restraint and sedation are required more frequently. Parent and provider perspectives were explored in order to better define facilitators and barriers to hospital based procedural care for children with ASDs.

Objectives: The primary aim of this needs assessment was to identify family and medical staff reported barriers and facilitators to hospital-based procedural care for children with ASDs. Secondary aims were 1) to identify differences in the needs and experiences of verbal versus non-verbal children with ASDs during hospital-based procedures, and 2) to identify strengths and deficiencies in hospital staff education regarding interaction with and assessment of individuals with ASDs.

Methods: We conducted semi-structured interviews with 20 parents of children with ASDs who had undergone hospital-based procedures and 21 medical providers working in the Sedation Unit at Children's Hospital of Philadelphia (CHOP). Participants were asked open-ended questions about factors they found facilitated or created barriers to successful interactions with children with ASDs and successful completion of the medical procedure. Interviews were audio-recorded, transcribed, coded, and analyzed for the emergence of major themes using the constant comparative method.

Results: The central theme that emerged is that individualized care is essential to quality care but is not consistently practiced. Parents and providers described a need for improved provider preparation and on-going communication with parents in order to enhance individualized care. They also identified a need for better provider

education on the approach to children with ASDs. Family and child preparation were seen as key to successful procedures as well, and as another area in need of improvement. Long wait times were recognized as a significant barrier to successful procedures. Participants, particularly parents, also felt there should be more accommodations made in the procedural environments (e.g. decreased noise/light, access to calming items) to facilitate successful procedure completion. There were no significant differences in needs identified by parents of children who were verbal versus those who were non-verbal.

Conclusions: Evidence shows that children with ASDs have more difficulty in the hospital setting and require more invasive interventions than other children to complete procedures. However, few training programs include instruction on how to work with children with ASDs, and few hospitals have interventions in place to aid in their care. This study suggests that improvements in child, family, and staff preparation and education as well as decreased wait times and environmental modifications can improve the quality and successful completion of procedures.

116.080 80 Helping Families Affected by Autism Fly. W. Ross*, *Einstein*

Background: Patient families affected by autism reported a reluctance to invest in air travel secondary to fears of negative experiences and reactions based on their child's atypical behaviors. An interdisciplinary team in Philadelphia created a program to help acclimate families affected by autism to air travel.

Objectives: To help families affected by autism to engage in air travel by preparing families for the experience, by preparing the air travel industry for the families, by training clinical staff to support community based efforts, and by creating and engaging in a practice experience that involves everyone.

Methods: We educated airport, airline, and TSA employees about autism in thirty-minute sessions that included pre and post surveys to ensure the efficacy of the intervention in increasing practical fund of knowledge. We prepared families for the experience with the use of tools like social stories and picture schedules. We prepared clinical staff to support families in the community. We

implemented a practice air travel experience, which includes doing everything from curb to cabin and back, with the exception of flying.

Results: We have had practice flights for over 50 families. Many of them subsequently had successful air travel experiences. We have worked with several airlines and currently have an international airline partner to help standardize and spread the program. We have educated over 300 airport, airline and TSA personnel about autism through thirty-minute educational talks with pre and post surveys that demonstrate improvement in fund of knowledge. We have additionally exposed personnel to children with autism through the practice sessions, leading Senator Lautenberg to add language to the 2011 appropriations bill requiring TSA engagement in practices for families affected by autism. We have been invited speakers by the Department of Transportation. We have involved over 25 clinical professionals of varying backgrounds, including medical, psychological, therapeutic, and educational. We are now creating curricula and tools to help standardize the application of clinical skills to community practice, especially for a population that may not be able to generalize abilities to new settings without support. We are working with the LEND program and presenting at AUCD with United Airlines, TSA, and DOT to help establish a standard in air travel inclusion for families affected by autism.

Conclusions: An intervention that involves preparing the airport, clinicians, and families can help facilitate air travel for families affected by autism. Families are seeking community experiences and value the components of preparation, supported practice, and educated community partners. A thirty-minute educational lecture can successfully educate community partners. Clinicians are seeking community-based application of their skills. Community partners are willing and supported by governmental forces to engage in supporting those affected by autism to engage in air travel. Next steps involve further developing the strategies and tools and creating a standard practice.

116.081 81 Evaluating and Enhancing Driving Skills of Individuals with Autism Spectrum Disorders. D. J. Cox*, S. M. Cox, R. J. Johnson, N. B. Cox, J. L. Wade, A. E. Lambert and R. E. Reeve, *University of Virginia*

Background: The ability to drive a car is paramount in the developmental process of achieving independence for adolescents and young adults. Symptoms of Autism Spectrum Disorders (difficulty with focus, limited attention flexibility, motor planning/coordination and a desire for structure and predictability) make learning to drive, and driving, particularly challenging for these individuals. However, limited research exists on driving safety among adolescents and young adults with ASD.

Objectives: Investigate the potential use of standardized Virtual Reality Training (VRT) to evaluate and train driving skills of individuals with ASD. Additionally, assess potential risk factors within this population including ASD symptomatology, anxiety, depression, and ADHD on driving performance and the procurement of a driver's license.

Methods: Fourteen subjects with ASD participated in an initial pilot study conducted during the summer of 2011; qualitative results helped to shape technological and study design improvements that have been implemented for the 2012 study, which began in late August. Our 2012 sample includes individuals with ASD (7 subjects to date, ages 15-25) who have secured a learner's permit from the DMV. Subjects were assessed at pretest using measures evaluating executive function (DKEFS, BRIEF), autism symptomatology (ADOS, SRS, SCQ), depression (CES-D), anxiety (BAI), and other associated behaviors (BASC-2). Participants were then matched on gender, extent of symptomatology, and type and degree of on-road training. Matched pairs were then randomized to either the control or the VRT group; controls did not receive any VRT. VRT involves 10 sessions of progressively demanding training. Both groups were given the *Department of Education 45-Hour Parent/Teen Driving Guide* to guide their on-road training at home. All subjects also kept logs of their on-road training and were evaluated pre and post training on VR operational and tactical driving assessments. Additionally, subjects received an on-road assessment by an independent DMV examiner at posttest.

Results: Qualitative results from our 2011 pilot study demonstrated a positive impact from VR training. At the conclusion of the ten sessions,

parents reported increased initiation of behind-the-wheel practice, described generalization of skills learned to real-world performance, and several participants obtained their driver's license. As recruitment and data collection are ongoing for 2012, quantitative analysis and conclusions regarding the potential effectiveness of the training program are unavailable at this time (posttests to begin October 28, 2012 and will be available well-ahead of conference). However, qualitative information supplied by the VRT instructor, participants, and their parents suggest improvement in driving skills and confidence for current VRT participants.

Conclusions: Limited empirical research and published findings highlight the need for additional studies on general driving safety within this population. Preliminary results of this study have demonstrated the feasibility of using virtual reality driving simulation as both an assessment and training tool for individuals with Autism Spectrum Disorders. While information gathered thus far is suggestive of positive outcomes, data collection is ongoing and more concrete results will be available by time of conference (early 2013).

116.082 82 Autism Comes to the Hospital: Experiences of Hospital Care From the Perspectives of Children and Adolescents with Autism Spectrum Disorders, Their Parents, and Health Care Providers. B. Muskat^{*1}, D. Nicholas², W. Roberts³, K. P. Stoddart⁴, L. Zwaigenbaum⁵ and P. Burnham Riosa¹, (1)*The Hospital for Sick Children*, (2)*University of Calgary*, (3)*University of Toronto*, (4)*The Redpath Centre*, (5)*University of Alberta*

Background: Children and adolescents with Autism Spectrum Disorders (ASD) are a vulnerable population who experience a multitude of mental health, developmental, and health challenges. Because of the complex presentation of ASD, these children and adolescents visit a variety of medical settings. During hospital visits, their special needs may be particularly high. Currently, there is a dearth of research examining children's experiences with hospitalization and even less on the unique hospital experiences of children and adolescents with ASD and their families.

Objectives: The purpose of this study was to understand the lived experiences of children and adolescents with ASD who were hospitalized, their

families, as well as those of paediatric health care providers (HCP) involved in their care. Ultimately, the findings will be used to inform policy and best practice approaches to the delivery of paediatric hospital-based health and mental health services for this unique and under-served segment of the population.

Methods: Semi-structured interviews were conducted with purposively selected children and adolescents with ASD ($n = 6$), parents ($n = 20$), and paediatric HCP ($n = 12$) who were central to their care at one of two large urban Canadian paediatric hospitals. Interpretive description, a qualitative methodology used to explore health research phenomena, was used to guide the analysis.

Results: Children and adolescents with ASD who were hospitalized for medical purposes and their families, indeed, faced unique challenges. Children with ASD experienced communication challenges *regardless* of their verbal ability, they had acute sensory needs, endured inflexible medical procedures, and expressed difficulties coping with change and waiting for procedures, tests, and appointments. Parents adopted the role of *child translator* in which they advocated strongly for their child's unique ASD-related needs. As a result, parents expressed a strong desire to be listened to and intimately involved in their child's health care decisions. Staff who maintained an open dialogue with the families, demonstrated sensitivity, appreciated the expertise of parents, tailored effective methods of communicating with the child, and displayed flexibility with procedures in small yet meaningful ways provided families with positive hospitalization experiences. Parents and HCP alike touted the value of staff training opportunities not only to understand ASD in general and appropriate support strategies, but more importantly, to develop an appreciation for the uniqueness of each individual and his or her unique hospital needs.

Conclusions: Through their lived experiences, children and adolescents with ASD, parents, and HCP provided important suggestions that will have wide-reaching utility for current hospital practices. As such, these findings are being used to develop a family- and staff-friendly resource to assist

families with children with ASD and staff prepare for hospital visits.

116.083 83 Transition to Mainstream Secondary School and Special Challenges for Children with an Autism Spectrum Disorder (ASD): Considerations Beyond the Triad of Impairments. M. Murin*¹, J. Hellriegel², S. M. Staunton³, O. Baykaner⁴, S. Anderson³, W. Mandy⁵ and D. H. Skuse³, (1)Great Ormond Street Hospital, (2)University College London, (3)Institute of Child Health, UCL, (4)Great Ormond Street Hospital for Children, (5)Faculty of Brain Sciences, UCL

Background: Transitions throughout education mark important developmental milestones, but negotiating transitions can be challenging for children with ASD, especially those with resistance to change. Difficulties in social interaction, communication and cognitive inflexibility all potentially influence success. Co-morbid disorders, such as ADHD, can exacerbate adjustment difficulties. The needs of children with ASD are not yet acknowledged by educational policies and practice.

Objectives: We aimed to assess, in a prospective study, the range and extent of difficulties faced by children with ASD transitioning between mainstream primary and secondary school. We wished to evaluate what additional support needs should be provided, and how the nature and severity of autistic traits influenced prospects of a successful transition.

Methods: Standardized assessments of 30 children (from 30 schools in UK) with ASD (mean age 11.28 yrs; SD0.4, mean IQ 88.79, SD17.48) were obtained from school and home visits prior to transition. Cognitive, executive and adaptive functioning were measured by WISC-IV, BRIEF and VABS-II respectively, plus the Beck Youth Inventory and the Parenting Stress Index.

Results: At initial evaluation, 89.3% had significantly discrepant cognitive profiles on the WISC-IV. We discovered a substantial difference existed between the children's relatively good cognitive abilities and their adaptive behavior, which impacted on their ability to handle the everyday demands of their school environment. Adaptive functioning was up to 6 years below their peers on the VABS-II: 30% were Borderline and 26.7% in the Mild Learning Disability range. Many had poorly developed executive functions (encompassing planning and organizational skills,

emotional regulation, and attention). 87% had Global Executive Composite scores (BRIEF) within the range of clinical concern. Comorbidity, including anxiety (41.4%), disruptive behavior (31%), anger (41.4%), and depression (41.4%) were significantly more common than expected from comparison data in this age group. Most (65.5%) had exceptionally poor self-esteem compared to their peers. 58.7% of families had clinically significant parenting-stress levels as measured by the Parenting Stress Index, usually exacerbated by concerns about managing their child's pending transition to secondary education.

Conclusions: ASD is cognitively a complex condition; measures of symptom severity and the degree of generalized learning difficulties do not fully reflect a child's individual needs and the potential risks associated with major life transitions. Many children in mainstream education do not successfully make the transition to secondary education and subsequently drop out, failing to achieve their potential as fully functioning members of society. Families need exceptional support at this time of transition, but few receive it; their stress levels are high. The importance for educational management of taking into account a complex cognitive profile (exceptionally poor working memory or processing speed for example), is emphasized by our study findings. Teachers are rarely aware of these issues and need education themselves about the impact of ASD on children's ability to learn.

116.084 84 A Systematic Review Examining ASD Vocational Practices, Supports and Models. D. Nicholas*, University of Calgary

Background: The Canadian *Participation in Activity Limitation Survey* (PALS, 2006) database suggests that adult males (25-64 years) with Autism Spectrum Disorder (ASD), have remarkably lower employment and labour force participation. It appears that only 40% of men with ASD are employed. Less than half participate in the labour force, i.e., either (i) employed or (ii) unemployed but looking for work. These employment outcomes are ~10% lower than that observed among other disabled male counterparts. Given these outcomes, it is not surprising that there is a substantial reliance on social assistance and disability benefits (PALS, 2006). Vocation-related service needs for adults with ASD have thus emerged with increased

urgency as a growing cohort of adolescents with ASD are aging into adulthood.

Objectives: This systematic review examined interventions addressing vocational services for adults with ASD.

Methods: This systematic review followed Campbell Collaboration standards in examining peer reviewed intervention literature related to vocational services for adults with ASD. Research questions were as follows: (1) What interventions supporting vocational opportunities for adults with ASD, are reported in the literature?, and (2) What evidence of outcome is indicated?

Results: Fourteen studies (1984-2011) met inclusion criteria for vocational focus on ASD and the presence of data. Studies identified 5 key areas of intervention, as follows.

(i) Supported employment: This involves the implementation of support to an individual with ASD in order to secure and maintain paid work in a regular work environment through formal training and ongoing workplace support.

(ii) Community placement: Placement in the community is supervised and supported directly by the employer. Additional support is provided as necessary, but is tapered over time.

(iii) Job coaching: 'Coaches' teach skills relevant to job searching and interviews, act as a liaison between individuals and employers/coworkers, deal with crisis situations, and generally seek to ensure the success of individuals with ASD in the workplace.

(iv) Technological support tools: Technology applications have been demonstrated to support vocational success for individuals with ASD (e.g., use of PDAs to improve independent functioning, and video modeling of job-specific vocational skills).

(v) Indirect vocational models: Programs for social skill development include non vocation-specific approaches that demonstrate improved social skills needed in the vocational setting. These are attributed to increased vocational opportunities, employment retention, and career advancement.

Conclusions: Existing studies demonstrate positive outcomes for identified interventional approaches. However, given the relatively weak study designs in existing studies, stronger methodology in future research is recommended. Future studies should increasingly address the role and importance of interpersonal relationships at work and how employment affects the development of identity and self-esteem. Labor market and economic analyses need to be implemented within future analyses. Notwithstanding these recommendations and yet unanswered questions, this literature base identifies promising vocational practices for further evaluation.

116.085 85 Transportation Research and Policy Review for ASD Individuals Across Canada: A Lifespan Perspective. J. H. Emery*¹, C. Dudley¹, D. Nicholas¹ and M. Clarke²,
(1)University of Calgary, (2)Sinneave Family Foundation

Background: The ability to travel efficiently, safely and reliability is fundamental to living a good life. Access to employment, education, recreation, leisure, and health care all rely on one's ability to get there. Challenges in transportation appear to exist for many living with ASD, yet much remains unknown as to how individuals with ASD get around, where problems exist and what conditions would improve transport situations.

Objectives: The goal of this project was to inventory policies and programs from Canadian provinces that exist to support persons with ASD in the area of transportation, to assess what is being done well, what is being missed and where promising policies or programs exist.

Methods: A systematic literature review by dual reviewers was completed to locate all peer reviewed literature regarding transportation and ASD. Grey literature documents were also examined for transportation related findings. Follow this, the researchers created a map of transportation needs for 3 hypothetical individuals on the spectrum through adolescents and adulthood. The individual case studies were of 1) A non-verbal individual with IQ under 70 and behavioral challenge 2) An individual with autism, IQ over 70 living with anxiety and depression 3) An individual with Aspergers Syndrome with social and sensory challenges. In consultation with local community groups the possible unmet

transportation needs were identified for each individual and different life stages. The researchers then searched government websites over a 4 month period using key words; autism, Aspergers, cognitive disability, and brain injury combined with transportation or travel.

Results: There is a gap in research and policy regarding transportation issues and needs for all individuals on the ASD spectrum. Grey literature consistently notes transportation as a barrier to accessing services. Several peer-reviewed research papers identified transport as a cost but only one paper documented the challenges of transportation, specifically of children and adolescents using special needs bus transport. Related research for those living with intellectual disability suggests that the use of IT strategies may assist some to increase independence. Transit systems are complex with most transit services and programs delivered at a municipal level. This results in different services and quality not only across provinces but within provinces. Municipal transit upgrades for disability needs were common, but were usually related to the needs of seniors, physical and sensory (visual and hearing) disabilities. Transit training programs were available in some municipalities but lacked information of strategies for ASD and challenging behaviours.

Conclusions: There is an extensive range of transportation challenges across the spectrum. There is an urgent need for more research, policies and programs to advance the transportation opportunities for adolescents and adults living with ASD.

116.086 86 A Transition Support Program for Young Adults with Autism Spectrum Disorders. K. White*, T. D. Flanagan and A. Nadig, *McGill University*

Background: The difficulties characterizing Autism Spectrum Disorders (ASDs) are often associated with childhood; however, ASD is a lifespan diagnosis impacting adulthood opportunities in the community (Graetz, 2010). Despite the need of continued services throughout the lifespan, there has been a focus on early interventions (Burgess & Gutstein, 2007). This childhood approach to research and intervention renders many young adults without proper support in other crucial outcome areas, such as independence and life skills. Given that the vast

majority of individuals with ASDs are still under the age of eighteen (Ouellette-Kuntz et al., 2005), these individuals will soon be adults and the significant gap in knowledge and transition support services have grave consequences for the individuals and their families (Howlin et al., 2004; 2012) and for society given the financial burden of long-term adult care (Ganz, 2007). A Transition Support Program was developed to cater to the specific needs in areas targeting communication, self-determination and social skills, which have been associated with better quality of life.

Objectives: We conducted a preliminary study to assess the effectiveness of a Transition Support Program in evaluation of communication, self-determination and social skills. This program was specifically catered to meet the needs of the young adults with ASD.

Methods: Six young adults with a high functioning ASD between 18 and 30 years old ($M = 23$, $SD = 2.97$) participated in the pilot phase of a quasi-RCT study with waitlist controls. A self-report questionnaire was used to assess their needs in communication, self-determination and social skills. The curriculum includes three modules with five sub-modules each:

1. Communication: Initiation, listening, perspective taking, making an impression, abstract and inferential language
2. Self-determination: Problem solving, self-regulation, choice making, self-advocacy, determining interests
3. Social (Working with others): Knowing your context (public/private), preventing and resolving conflict, who are good partners for interaction, getting the bigger picture, teamwork

The curriculum was developed to meet the collective needs of the participants. The young adults participated in a two-hour group program co-led by two facilitators for ten weeks. A program evaluation questionnaire asking participants to self-report their pre- and post-program skill levels across the three modules was administered.

Results: All young adults met the diagnosis for an ASD based on the *Social Communication*

Questionnaire and the Autism Diagnostic Observation Schedule. Based on the needs assessment, the curriculum was developed to include the following modules:

1. Communication skills: listening, making an impression, and initiation
2. Self-determination skills: developing preferences, interests and strengths, self-advocacy, self-regulation, and problem solving
3. Social (Working with others): knowing your context (public vs. private), and what makes good partners

Participants reported lower skills before the program across the three modules, followed by medium to higher skills post-program. Overall, participants found the program to be informative and a positive experience. Implications for policy will be discussed.

Conclusions: The intervention introduced in this study appears to be effective and socially valid. However, more research is needed on transition services required to meet the needs of people with ASD across the lifespan.

116.087 87 Coming of Age: Examining the Transition From Child to Adult Services for Persons with Autism. M. Milen* and D. Nicholas, *University of Calgary*

Background:

Autism Spectrum Disorder (ASD) presents pervasive challenges across the lifespan. Systems of support exist for children affected by ASD, yet there are few resources available to assist youth and young adults with ASD during the transition to adult care. With an exponential growth in the number of young persons diagnosed with ASD moving into adulthood, it is important to consider the multidimensional shifts and changes associated with this transition for the individual, his or her parent/caregiver, care planning, service resources, and vocation and education. Inherent to these processes are multiple barriers, opportunities and disruptions that may require substantial adjustment, work, and time to understand and coordinate. The transitional period can be further confounded by impaired physical or mental abilities, pain, health setbacks, forced

dependence, misconceptions about condition, and perceived outcomes and care needs. The combination and overlap of these factors that may occur simultaneously can render transitions extremely difficult, warranting comprehensive and individualized planning for young persons with ASD.

Objectives:

This study sought to understand: (1) needs, facilitators, and gaps related to transition, (2) key junctures of transition, and (3) perceived strategies for effective transition planning.

Methods:

Utilizing McCracken's *Long Interview Method*, 11 in-depth, semi-structured interviews were conducted with young persons (16-25 years of age) with ASD and/or her or his parent(s). A purposive sampling approach based on criteria of maximum diversity was used to ensure diversity across symptom severity and family demographics. Broad, open-ended questions were used in the exploration of the perspectives of both young persons and parents. Interviews were subject to concept saturation and theme generation, assisted by qualitative data analysis software (NVivo).

Results:

Data analysis is underway; however, several preliminary themes common to participant families have emerged, including: (1) key transition points at age 18, with the individual coming of legal age; and at age 20, when the individual is required to complete their final year of secondary education; (2) a dearth of systemic supports or resource guides to assist in navigating unfamiliar adult-based systems of care; (3) a marked end of regimented day programming and opportunities similar to the individuals' neurotypical peers; (4) difficulty in obtaining and maintaining qualified and knowledgeable aides for the individual with ASD; and (5) despite the difficulties associated with the transition to adulthood, individuals and parents held hope for improved services and opportunities for adults with ASD.

Conclusions:

This study provides an understanding of the needs, facilitators, and gaps related to adult transitions from the perspective of both individuals with ASD and their parent(s). This information can be utilized to improve transitional and adult focused programs and services for individuals with autism and their families.

116.088 88 The Impact of Autism Services On Mothers' Workforce and Leisure Participation and Wellbeing. S. Hodgetts*¹, D. McConnell¹, L. Zwaigenbaum¹ and D. Nicholas²,
(1)University of Alberta, (2)University of Calgary

Background: Autism is a pervasive neuro-developmental disorder that affects the entire family system. Professionals often work with families to address the needs of the child with autism, yet the needs of parents are rarely addressed even though their participation in meaningful activities may improve child development.

Objectives: To investigate the impact of professional services on mothers' ability to participate in personally meaningful employment and leisure activities, and the relationship between service characteristics and maternal wellbeing.

Methods: A sequential, mixed-methods approach was used. N=139 mothers of children (age 2-29 years) with autism completed a detailed questionnaire including: (1) detailed child, mother and family demographic information; (2) detailed questions on maternal employment and leisure participation; (3) professional service information including frequency of contact, number of professionals, and service location (*Education and Rehabilitation Services Questionnaire*; Remple, Rogers & Majnemer, 2010), continuity of services over time and across sectors (*Alberta Continuity of Services Scale for Mental Health*, Adair et al., 2001), perceptions of family-centered care (*Measure of Processes of Care*, King et al., 2004); and (4) indicators of maternal well-being, including the *Perceived Stress Scale* (Cohen et al., 1983) and *Parenting Sense of Competence Scale* (Gibaud-Wallston & Wandersman, 1978). A sub-sample of 20 mothers who completed the questionnaire, purposefully sampled for diversity in child and family characteristics, participated in

a semi-structured interview to discuss their experiences in more depth.

Descriptive statistics, including demographic information, supports and services data, and employment and leisure data were calculated to describe the sample and test the impact of professional services on employment and leisure participation. Path analysis was employed to determine the impact of professional services on maternal wellbeing, and potential child, mother or family variables that may influence outcomes. Qualitative interviews were content analyzed using constant comparison methods consistent with a grounded theory approach (Creswell, 1998; Strauss & Corbin, 1998).

Quantitative and qualitative findings were integrated to contribute to a formative understanding of the impact of professional services on mothers' participation and wellbeing.

Results: Preliminary results indicate that professional services decrease mothers' ability to participate in the paid workforce and personally meaningful leisure activities, even as children became older. Controlling for parent-perceived need and frequency of services, we found that higher number of professionals, discontinuity of services, and home-based services were significantly associated with decreased maternal wellbeing. We found no statistically significant association between perceptions of FCC and maternal well-being.

Conclusions: This study suggests that mothers' sacrificing their own participation and wellbeing for professional services for their child with autism. Since maternal wellbeing, positively associated with mothers' participation in personally meaningful activities, can positively affect child development and wellbeing, a focus on participation and wellbeing of mothers of children with autism may have collateral benefits for the entire family.

116.089 89 Service Needs of Adults with Autism. D. Johnson*¹, A. Singer¹, C. Anderson², P. A. Law³ and J. K. Law³, (1)Autism Science Foundation, (2)Towson University, (3)Kennedy Krieger Institute

Background: Autism is a pervasive developmental disorder that persists into adulthood, yet there is

little research available on the trajectory of autism over the life course. Behavior and symptoms change as children with autism mature into adults, resulting in new challenges and needs for this population. Little is known about the unique service requirements of adults with autism, underscoring a significant need for data to help guide the development of relevant and useful services that may improve quality of life.

Objectives: The primary aim of this study was to learn more about the needs of adults with autism by identifying the drivers of fulfillment and success in employment, leisure, and spirituality. A secondary objective was to determine whether the needs and success drivers reported by adults with autism are the same or different from the needs and success drivers reported by parents of adults with autism.

Methods: The Autism Science Foundation (ASF), UJA-Federation of New York (UJA), and the Interactive Autism Network (IAN) collaborated to develop an online questionnaire to survey the needs of this population. The survey included 68 open and closed ended items, focusing on a range of topics including education, employment, and leisure activities. Contingency items were used to further explore responses where applicable. A hyperlink directing respondents to the survey was disseminated via email, social media platforms, and mailing lists. A convenience sampling method was used: ASF and UJA informed prospective participants and organizations of the survey's impending release and interested individuals registered to receive or distribute the survey once IRB approval had been received. Respondents who did not pre-register but were made aware of the survey through word-of-mouth, email, networks, or social media were still eligible to participate. Participants fell into one of three categories with an enrollment goal of 100 per group: independent adults with ASD not under legal guardianship and between the ages of 18 and 35; parents of an independent adult with ASD aged 18-35; and legally authorized representatives (legal guardians) of a dependent adult with ASD aged 18-35. The survey was open for responses for a two-month period.

Results: Data are expected to be reported in December, 2012.

Conclusions: To our knowledge, this is the first large-scale investigation that has systematically examined the vocational, social, and spiritual needs and experiences of autistic adults, and incorporated the perspective of parents and legal guardians. The results from this study will provide a more nuanced understanding of the challenges autistic adults and their parents face, and what success means to them. Moreover, this study has the potential to yield much-needed, actionable information on how best to serve and support this population. Ultimately, we envision that the results will help clinicians, advocates, and stakeholders make data-driven decisions with regard to programs and therapies for autistic adults.

116.090 90 An Assessment of Needs to Guide a Transition Support Program for Young Adults with ASDs. T. Flanagan*, A. Nadig and K. White, *McGill University*

Background:

There is a very significant gap in support services for young adults with Autism Spectrum Disorders (ASDs). Lack of support in the transition between secondary school and adulthood may have consequences both for individuals with ASDs and their families in terms of employment and social inclusion (Howlin, 2005). As Burgess and Gutstein (2007) highlight, the proliferation of ASD diagnoses has not been met with an increased interest in the lifespan development of persons with ASDs nor in their quality of life (QOL) which may leave many adolescents and young adults without proper support and scaffolding in other crucial outcome areas associated with successful transitions into adulthood (McGovern & Sigman, 2005).

Objectives:

To establish participant needs in the creation of a transition support program for young adults with ASDs. To explore the use of QOL as a possible outcome measure of intervention with young adults on the spectrum.

Methods:

Participants in this pilot phase of an RCT transition support program were 6 young adults (3 females) on the ASD spectrum, aged between 18 and 30 (M

= 23, $SD = 2.97$), who all met criteria for an ASD based on the *Social Communication Questionnaire* (SCQ; Rutter, Bailey, & Lord, 2003) and the *Autism Diagnostic Observation Schedule* (ADOS; Lord, Rutter, DiLavore, & Risi, 1999).

Participants completed a needs assessment questionnaire and the Quality of Life Questionnaire (QOL.Q; Schalock & Keith, 1993). The needs assessment questionnaire consisted of open-ended and Likert-type questions regarding desired topics, instructional strategies, learning styles, and assessments of needs and skills (low, medium, high) in the areas of communication, self-determination and working with others. The QOL.Q has 4 subscales: Satisfaction, Competence/Productivity, Empowerment/Independence, and Social Belonging/Community Integration and scores are combined into an overall QOL score.

Results:

In response to the open-ended questions, participants reported interest in learning more about decision-making processes, managing change or unexpected situations, managing social interactions in the workplace, and exploring interests. Most reported learning best in small groups, in quiet environments, through the visual modality and through hands-on approaches such as role-playing. The participants mostly reported mid range skills and needs in the areas of communication, self-determination, and working with others. But, self-determination skills were mentioned in the high needs category by 50% of the participants.

The program curriculum was tailored to the group based on the results from the needs assessments, and the material was differentiated accordingly. The 6 young adults then participated in weekly two-hour small group sessions for ten weeks. QOL assessments were completed pre and post program. The pre-program QOL scores varied among the participants though all were commensurate with or higher than the scores reported for the norming sample. The pre/post QOL patterns seem highly nuanced and are explored further in a figure.

Conclusions:

The results from this pilot study point to the utility of data from needs assessments for interventions and for more accessible curricula for young adults on the spectrum. QOL as an intervention outcome needs further exploration but has implications for transition programs.

116.091 91 The Efficacy of Person-Centered Planning for Young Adults with ASD in Transition. M. Magnee*¹ and J. P. Teunisse², (1)*Hogeschool van Arnhem en Nijmegen*, (2)*Dr Leo Kannerhuis*

Background: For many young adults with autism spectrum disorders (ASD), the transition into adulthood (e.g. educational, employment or independent living) can be particularly stressful. Positive transition outcomes therefore necessitate careful transition planning. Person-Centered Planning (PCP) refers to a number of different transition planning approaches, all of which share the belief that the person at the focus of the planning is also the primary authority on his or her life direction. Although PCP is widely used in the field of intellectual and developmental disabilities, there has been little evidence on its efficacy for individuals with ASD.

Objectives: Our objective was to study the efficacy of Person-Centered Planning for individuals with ASD as they make the transition to independent living. Our aim was to re-evaluate the data every 3 months for 1 consecutive year, in order to identify the most discriminating factors of PCP leading to a positive transition outcome.

Methods: We recruited six young adults with ASD (two females, four males; mean age 22.5 years) before they made the transition to independent living. All participants were residents of the living lab 'E-Xperience', where several health innovations in care for individuals with ASD are brought together. Measures were obtained of autism conditions (AQ), quality of life (QoLC), self determination (AIR), psychological well-being (SCL-90), social network analysis (MSNA), and goal attainment scales (GAS). These questionnaires will again be administered at 6- and 12-months follow up. Further, we aimed to undertake comprehensive assessments of the different components of the PCP process and re-evaluate this information every 3 months for 1 consecutive year in order to identify the most discriminating predictors of outcome. We used the MAP (Making Action Plans; Forest & Snow, 1992)

as a procedure for PCP. This procedure was evaluated by means of a checklist "How Person-Centered was this planning process" (Hagner et al., 2012).

Results: All PCP sessions were completed and between 3 – 5 goals were set for each participant. The number of people involved with the implementation of the plan varied between 3 and 6. Preliminary linear regression analyses revealed a strong inverse correlation (-0.92) between the number of people involved with the implementation of the plan and the satisfaction with the plan 3 months after the PCP session ($F = 22.1$; $p < 0.01$). Additional 6- and 9-months follow-up data together with in-depth qualitative information from personal interviews will be presented at the conference.

Conclusions: Implications for this study include an improved understanding of the efficacy of Person-Centered Planning for individuals with ASD as they make the transition to independent living. Highlighting these issues elicits the potential to produce more rigorous research into the effectiveness of PCP for individuals with ASD and make a more efficient translation from research to practice. Preliminary results at three months follow-up indicate that group size during the PCP session negatively impacts satisfaction with the plan. Follow-up on these data and on the comprehensive information from questionnaires and interviews will be presented at the conference.

116.092 92 Crisis in Adults with Autism Spectrum Disorders: Antecedents and Outcomes. C. A. McMorris*¹, J. K. Lake² and Y. Lunsky², (1)York University, (2)Centre for Addiction and Mental Health

Background: A crisis is defined as *an acute disturbance of thought, mood, behaviour, or social relationship that requires immediate attention as defined by the individual, family or community* (Allen, et al., 2002, pg 8). The negative impact of crisis for individuals with Autism Spectrum Disorder (ASD) and their families has been well documented in previous research. Given individuals' with ASD social, communicative, and behavioral impairments, crisis can often lead to involvement with the criminal justice system (Woodbury-Smith, et al., 2006; Allen et al., 2008), loss of residential placements, serious injury, and admission to

psychiatric facilities (Hardan & Sahl, 1999; Lokhandwala, et al., 2012; Palucka & Lunsky, 2007; Puddicombe & Lunsky, 2007). Despite the negative impact of crisis, there is limited research examining what leads to crisis in this population as well the outcomes, types, and severity of these crises.

Objectives: To describe the type, antecedent, outcome, and severity of crises in a clinical sample of Canadian adults with ASD. We also examine whether particular antecedents predict specific crisis types and outcomes.

Methods: As part of a larger project examining behavioural crises in adults with developmental disabilities, crisis information was collected on 214 adults with ASD from three urban centers in Ontario, Canada. Each of these adults experienced either a psychiatric or behavioural crisis and was served by participating social service or mental health agencies for people with developmental disabilities. Agency staff recorded information related to the crisis, as well as other demographic and clinical information (e.g., life events, medication use, risk behaviours, service use, comorbid medical and psychiatric conditions). Crisis antecedents were classified according to 3 categories; autism symptoms (e.g., interpersonal difficulties, challenges with transition, rigid/restrictive behaviour issues, communication problems); medical and psychiatric comorbidities (e.g., medication changes, medical problems, mental health issues); and life changes (e.g., deterioration of supports, life events).

Results: Preliminary analyses indicate that the most common types of crises for adults with ASD were physical threat (50.7%), suicidal behaviour (9.4%), and property damage (8.0%). Crisis antecedents were also analyzed for 68 of the 214 crises. Autism symptom antecedents were the most common (23.8%), followed by medical and psychiatric comorbidity antecedents (10.3%), and life change antecedents (5.6%). For 18% of our sample, their crisis led to an emergency department visit. For these individuals, the most common crisis outcomes were inpatient admission (57.9%), overnight admission (32.4%), and new medications (27.0%). Results of regression analyses will be discussed.

Conclusions: Results from the present study indicate that adults with ASD experience a variety of behavioral crises, with physical threat being the most common. The most common crisis antecedents stemmed from autism symptoms, and outcomes for individuals who went to the emergency department most often resulted in an inpatient admission. Understanding what leads to and results from behavioural and psychiatric crises in adults with ASD may help to inform the development of appropriate, crisis-specific supports for adults with ASD, as well as, crisis prevention and intervention programs.

116.093 93 Findings From the Insar Special Interest Group: Global Knowledge Translation for Research On Early Identification and Intervention in Autism. A. A. Yusuf*¹, S. Prasanna¹, L. G. Anthony², T. Charman³, B. A. Malow⁴, C. E. Rice⁵, A. Shih⁶, H. Tager-Flusberg⁷, P. de Vries⁸ and M. Elsabbagh¹, (1)McGill University, (2)Children's National Medical Center, (3)Institute of Education, (4)Vanderbilt University, (5)National Center on Birth Defects and Developmental Disabilities, (6)Autism Speaks, (7)Boston University, (8)University of Cape Town

Background: Autism remains under-diagnosed in many communities across the world, and especially where priorities include issues of survival and physical health (Khan et al., 2012). Research plays a critical role in supporting and enabling community-based efforts in early identification and intervention (Elsabbagh, 2012). The INSAR special interest group (SIG) "Global Knowledge Translation for Research on Early Identification and Intervention in Autism" was formed in 2011 to support mapping of community needs in this area.

Objectives: The inaugural meeting of the SIG was focused on sharing global perspectives on community-based approaches in early identification and intervention and gathering suggestions for future research priorities.

Methods: Participants in the inaugural SIG were 90 international clinicians and researchers. During a 40-minute session, subgroups of participants (8-10 per group) discussed the following thematic priorities in supporting early identification and intervention: (a) Enhancing community awareness and public engagement, (b) Supporting informed decision-making and evidence-based practice, (c) Building research capacity in under-resourced communities, (d) Implementation of evidence-

based public policy. Content domains and items were generated from subgroups' written notes. We identified emerging themes from the discussions and determined the priority of each theme from the frequency of discussion across groups.

Results: Some factors that impede early identification and interventions in diverse community settings appear to be systemic such as the lack of resources and limited knowledge and training among primary health care and education professionals. Other factors are cultural, including pervasive stigma and misconceptions regarding the biological basis of autism. Capacity building efforts in some communities have relied on linguistic translation of screening/diagnostic tools, intervention manuals, and support programs developed in high-income communities. While some participants view such approaches as essential, others cautioned that translation has often undermined the importance of culturally-sensitive and contextually-relevant adaptation addressing the needs and priorities of diverse communities. Examples of priority areas for action include (a) empowerment and engagement of families and community stakeholders, (b) enhanced understanding of diverse communities' priorities, capacity, and resources, (c) supporting the integration of identification programs within existing health and educational systems, (d) pairing awareness and identification programs with support for those affected, and (e) adopting broader child health/education/human rights perspectives that encompass a range of developmental conditions as well as autism.

Conclusions: Over the next two years, the SIG will offer a vehicle supporting dialogue and sharing of knowledge from diverse communities in the area of early identification and intervention.

Acknowledgement: We are grateful to the participants of the SIG for expressing their views and sharing their experience.

116.094 94 Cultural Considerations in Autism: A Comparison of Autism Experiences in Kerala, India and Atlanta, GA USA. J. C. Sarrett*, Emory University

Background: Autism as a concept and diagnosis is increasingly recognized around the world, however little is known about how various cultural elements may impact the lives of those living and

working with autism. Assuming that the ways autism is talked about, conceptualized, and treated is universal can lead to improper diagnoses and treatments and damage beneficial, collaborative relationships for research, intervention, and advocacy. This work can be improved by gaining a deeper understanding of the ways culture and autism intersect.

Objectives: This project uses cross-cultural, qualitative research methods to identify critical variations in outcomes related to quality of life for children with autism and their families. These outcomes are then analyzed in relation to specific cultural elements most influential to differences in how autism is identified, treated, and understood to develop a model for how to improve the efficiency of future international autism work.

Methods: Thirty families and 45 professionals in Kerala, India and 17 families and 19 professionals in Atlanta, GA USA participated in the current research. Interviews and observations were conducted from June to December of 2011 in Kerala and March to September of 2012 in Atlanta. As autism is a new diagnosis in Kerala, the research included families of children who exhibited significant traits of autism yet who may not have an actual diagnosis. This caveat ensured the recruitment of comparable populations and the inclusion of possibly neglected families. Professionals were required to have been interacting directly with children with autism for at least 1 year and included physicians, psychiatrists, traditional healers, educators, and therapists. Grounded theory was used to identify common themes, which are then compared across and within each research site.

Results: Data analysis is ongoing, however preliminary results show that variations in access to resources, the ways people explain autism (explanatory models), and expressions of stigma are some of the most important areas of difference across the cultures researched. These, and other outcomes yet to be identified, will be analyzed alongside important cultural elements, such as nation, class, familial structure, treatment options, and urbanicity, to discuss the ways researchers, interventionists, and advocates can improve the efficiency and effectiveness of international autism work.

Conclusions: Although the current research is not fully completed, implications are far reaching. This work will improve international work and can also aid in interactions with diverse populations within our own communities. Additionally, this work can

be extended to children with a variety of intellectual and psychiatric differences. This work not only fills a gap in the autism literature, but also one in medical anthropology where both autism and conditions of childhood are often neglected. The model created through this research will be easily followed by anyone embarking on autism work in diverse and international communities and will ensure this work is done with sensitivity and competence.

116.095 95 An Autism Spectrum Disorders (ASD) Database:

Regional Pilot for a National ASD Database for Wales, UK.
S. R. Leekam*¹, D. Wimpory² and B. Nicholas³, (1)*Cardiff University*, (2)*Bangor University and Betsi Cadwaladr University Health Board*, (3)*Bangor University*

Background: It is important to have precise information about the prevalence and demographics of service users with ASD. This can help service providers and policy makers to recognise current needs of ASD populations and thereby develop and target suitable services. This project developed a database for this purpose. Prior to the implementation of this database project, not all ASD diagnostic results were being recorded accurately and there was a lack of detail on each ASD diagnosis.

Objectives: 1) To develop and pilot a regional database in preparation for national rollout across Wales, UK. This database aims to provide 100% coverage of the regional health board child population with accurate ASD diagnostic records, 2) To assess how well ASD was reported before this pilot, and 3) To examine the prevalence of ASD in the regional area after the implementation of the ASD database project.

Methods: A module was created to record details of ASD diagnosis within an existing electronic database (the Child Health Database: CCH). Module development included the design of new software to support the new module. Additionally, changes in policy and procedure were implemented. The resulting ASD Diagnostic Report Form was developed and adopted as part of the regional health board's Minimum Standards for Assessment and Diagnosis of ASD.

Results: Before implementation of the ASD database project, an average of 1 diagnosis per month was recorded. Following implementation of the project, for the first six months of 2012, an

average of 14 diagnoses per month were recorded. However, occurrence of common genetic co-morbid disorders (e.g. fragile X syndrome and Phenylketonuria (PKU) are well below statistically expected levels. In 2009, before the project started, 88% of ASD diagnoses in the regional healthboard were not being recorded. Following implementation of the project, more than 60% of diagnoses were being appropriately made by more than three collaborating disciplines. The most frequent collaborators were clinical psychologists, nurses, and psychiatrists. 52% of clinicians in the BCUHB used more than one standardised tool to assist the diagnosis, with ADOS being used for 65% of cases.

Conclusions: This project has provided a process for ensuring good practice for recording ASD cases on an existing database and has already demonstrated improvements in the rate of reporting. It is most important to prioritise the progression of the ASD database from regional pilot to national roll-out across Wales. Furthermore, the ASD database has already recorded over 1000 cases and will provide potential for clinical and scientific analysis in the future.

116.096 96 Re-Mapping Autism Research in the UK: Identifying Priorities for the Decade Ahead. T. Charman¹, E. Pellicano² and A. P. Dinsmore^{*1}, (1)*Institute of Education*, (2)*Centre for Research in Autism & Education*

Background:

The recognition that autism is more prevalent than was previously realised has been accompanied by an increase in research interest. An accurate summary of the autism research landscape is required to ensure that decisions made about future priorities are appropriate and well informed, particularly given the fierce competition for research funds in the current economic climate.

Objectives:

The aims of this study are (1) to provide a comprehensive summary of the current state of autism research (in terms of both grants awarded and published articles) in the UK and internationally; and (2) to seek the views of a wide

range of individuals from the autism community regarding their priorities for future research.

Methods:

We used two streams of inquiry to address objective 1. First, 12 online journal databases were searched for articles containing any of a selection of autism-related search terms in their title, abstract or key words published in 2001 and 2011 to compare changes over the past decade. Second, a similar search was conducted on online research funding databases for funding awards made between 2007 and 2011 in the UK, Ireland, USA, Canada, Australia and New Zealand. The primary topic of all articles and funding awards identified were systematically categorised with a protocol adapted from previous work.

To address objective 2, interviews and focus groups were conducted with a broad range of stakeholders including autistic people, parents of autistic children, autism researchers and autism practitioners to identify participants' priorities for future research. The views and perspectives of a large number of stakeholders were also captured via an online survey.

Results:

Data collection in each of the four data streams is ongoing. Provisional findings include:

1. 1,463 and 4,727 academic articles on autism were published in 2001 and 2011 respectively.
2. 115 funding awards were made in support of autism research in the UK between 2007 and 2011 comprising a total spend of £21.2m and an average annual spend of £4.2m – relative to the \$408.6m (£251.8m) spent in the USA in 2010 alone.
3. Early-career researchers and parents of autistic children agreed that current knowledge about autism in adulthood in particular is insufficient and that research into this area should be prioritised in future.

Conclusions:

These preliminary results indicate that peer-reviewed autism publications tripled in number between 2001 and 2011 and that both real and per capita spending on autism research in the USA far exceeded that in the UK between 2007 and 2011. Themes generated from the focus groups conducted so far provide intriguing insights into how the priorities of researchers and non-academics overlap and diverge, which will be augmented by the findings of the online survey launched in November 2012.

116.097 97 A UK Survey of Families' Opinions of Health Services and Treatment Priorities. S. B. Wallace*, *Autistica*

Background: There remains a lack of data published in the literature about families' (parents of children with autism and adults on the autism spectrum) experiences of the health system and what areas of medical research they would like scientists to focus on. One priority area for future health services research would be to improve the experiences of families around the time of diagnosis. Additionally, it will be important to gather families' opinions about treatment options that are currently available or may be in the future.

Objectives: To survey parents of children and adults with autism, as well as adults on the autism spectrum, regarding their experiences: 1. at the time of diagnosis; 2. of current treatment options.

Methods: UK autism research charity, *Autistica*, and Newcastle University designed and circulated a survey that was open to UK residents during September and October 2012. The questions could be completed by parents (of either children or adults with autism) or adults on the autism spectrum. The survey was accessed online, it took approximately 15 minutes to complete and was sent out via national and regional contact databases.

Results: At the time of writing this abstract, 1044 respondents (869 parents; 175 adults with autism) had so far completed part or all of the survey. Just under half (46.5%) of parents and two thirds of adults (67%) had seen their family doctor about their child's/their own autism, with mixed experiences. Approximately half (48%) of parents and adults with autism (49%) felt they received enough information at the time of

diagnosis. One third of parents (33.2%) and slightly more adults with autism (37%) responded that they had talked to someone on the autism spectrum at the time of diagnosis and found it helpful. 65% of parents and 56% of adults with autism reported concerns about using medication to help with issues such as anxiety or sleep, and mainly commented on previous bad experiences or worries about side effects. 64% of parents reported being ready to access interventions for their child immediately after diagnosis and 22% would want to wait one month or more. In terms of interventions to support adults on the autism spectrum, parents prioritised help with social skills (89%) and adults with autism prioritised help with stress (79%) and greater understanding from the public (79%).

Conclusions: The data from this survey so far indicates a mixed response in terms of families receiving enough and reliable information from healthcare providers at the time of diagnosis. Anxieties about the use of medication and different preferences in terms of when interventions should commence, must be taken into consideration when developing treatment plans. Future research should also be mindful of the different preferences parents and adults with autism have in terms of the focus of interventions.

116.098 98 Challenges Facing Educators of Children with Autism in Oman From Educators' Perspective: A Qualitative Study. Y. M. Alfarsi*¹, M. F. Al-Said², M. M. Al-Khaduri¹, M. Al-Sharbati¹, M. I. Waly³, M. Al-Shafae⁴, A. Ouhit¹ and S. al-Adwai¹, (1)*Sultan Qaboos University*, (2)*Sultan Qaboos university*, (3)*S.Q.U.*, (4)*squ*

Background:

Educating children with autism spectrum disorder (ASD) is challenging, especially in developing countries where awareness about ASD is broadly considered low. Also, developing countries suffer from dearth of scientific evidence that explore factors hampering the quality of service especially those related to local cultures.

Objectives:

To explore the educators' views towards hampering factors of delivering high-quality education to children with ASD in Oman, an Arab country in the Middle East.

Methods:

Semi-structured face to face interviews were conducted among 20 autism educators recruited in two selected centers caring for autism in Muscat Region, the capital of Oman. The qualitative data were analyzed using a framework approach.

Results:

Several hampering factors were identified by educators which affect the quality of service. The main reported hurdle is lack of a standard curriculum in Arabic that has been standardized to the local culture. Other obstacles noted were: limited teaching resources, restricted space available, shortage of supportive staff, inconsistent transportation, and the need for trained dietitian for dietary consultations. The educators reported also the urgent need to educate the general public about ASD and to rectify for common misconceptions.

Conclusions:

Educators of children with ASD face many challenges related to availability of resources, communication with the society, and the need for logistical support. Governmental and non-governmental authorities are called to consider these challenges from educators perspective, and work on developing a standard curriculum, and provide multi-disciplinary integrative services that would overcome the challenges.

116.099 99 Predictors of Early Intervention Service Utilization

Among Children with Autism. E. R. Hotez^{*1}, M. Siller², N. M. Reyes³, T. Hutman⁴ and M. Sigman⁴, (1)*The Graduate Center of the City University of New York*, (2)*Hunter College of the City University of New York*, (3)*Virginia Tech*, (4)*University of California, Los Angeles*

Background: The National Research Council recommends that children with Autism Spectrum Disorders (ASD) should receive a minimum of 25 weekly hours of intervention, although it is estimated that fewer than 1 in 10 children with ASD receive appropriate services (NRC, 2001). Data from a national survey of Early Intervention Coordinators suggest that in almost half of the reporting states (44%), children with ASD typically receive five or fewer weekly service hours

(Wise et al., 2010). Additionally, descriptive research reveals large individual variation in families' utilization of community services. Only a few published cross-sectional studies have investigated whether this variation in service-utilization can be attributed to family demographics (Irvin et al., 2012; Thomas et al., 2007).

Objectives: The current study aimed to evaluate family demographic factors (i.e., household income, ethnic/racial background and parental education) associated with the intensity (hours/week) of children's early intervention services during the first three years of life for children with ASD.

Methods: This research involved 70 largely nonverbal children with ASD (chronological age: M=58.3 months; SD=12.7). The researchers confirmed children's ASD diagnoses with the Autism Diagnostic Observation Schedule-Generic (ADOS-G; Lord et al., 2000) and the Mullen Scales of Early Learning (MSEL, Mullen, 1995). Children's early intervention service utilization was evaluated using a retrospective structured parent interview (Bono, Daley, & Sigman, 2004) that asked parents about services children received during their first three years of life. Parents were also asked to complete a demographic questionnaire that included questions about the child's ethnicity/race and various indicators of the families' socioeconomic status (i.e. annual household income, parents' educational attainment). Change in service utilization was analyzed through mixed models analysis for longitudinal data (SAS Proc Mixed).

Results: The percentage of children who received less than 1 weekly hour of individual services was 100%, 90%, and 57% during children's first, second, and third year of life. While no children received more than 5 weekly hours of services during children's first 2 years of life, 13% of children received between 5 and 20 weekly hours of services during children's third year of life. Results from mixed model analyses revealed that the rate of change in children's weekly hours of individual services (log-transformed) were predicted by several indicators of socioeconomic status, including annual household income, $F(1,132) = 6.95$; $p < .01$ and ethnic/racial background, $F(1,134) = 6.43$; $p < .05$.

Interestingly, children's service programs during the first three years were not predicted by the parents' educational attainment (n.s.).

Conclusions: African American and Hispanic families as well as families with lower annual household incomes had lower utilization of individual early intervention services. Future research would benefit significantly from adding observational measures that also evaluate qualitative differences between children's early intervention programs.

116.100 100 Using Evidence-Based Diagnostic Practices to Identify Autism Spectrum Disorders in Youth Served in Community Mental Health Settings. N. Akshoomoff*¹, N. Stadnick², L. Brookman-Frazee¹, K. Nguyen Williams³ and G. Cerda¹, (1)University of California, San Diego, (2)SDSU/UCSD Joint Doctoral Program in Clinical Psychology, (3)Rady Children's Outpatient Psychiatry, San Diego

Background: School-aged children with autism spectrum disorders (ASD) are increasingly served by the community mental health (CMH) system given their high rates of co-occurring psychiatric problems (e.g., anxiety, mood, attention, disruptive behaviors). The CMH system may also help to identify ASD in school-aged, higher functioning children with diagnostically complex presentations. However, research suggests that a significant number of clinicians in community-based settings do not use best diagnostic practices to assign an initial ASD diagnosis (Wiggins et al., 2006; Williams et al., 2009). Due to the clinical complexity of these children, limited training in or use of evidence-based diagnostic practices by CMH providers, and the significant proportion of these youth from minority or non-English speaking families, identifying children with ASD in CMH settings is challenging (Mandell et al., 2002). Limited research therefore exists on the feasibility of identifying ASD using evidence-based diagnostic practices and the characteristics of children referred for ASD assessment in CMH settings.

Objectives: This study's aims were to: 1) examine the characteristics of children served in a CMH clinic who received an ASD assessment from providers trained to use the Autism Diagnostic Observation Schedule (ADOS) and 2) identify the clinical characteristics associated with receiving a final ASD diagnosis in this setting.

Methods: Data were extracted from CMH clinical records (psychodiagnostic reports). CMH clinicians from three affiliated clinics referred children receiving services (therapy or therapy plus medication management) who were suspected of ASD based on results from screening measures and clinical judgment. Eighteen CMH clinical psychologists and psychology trainees were trained by an experienced and certified ADOS trainer and conducted ASD assessments. The ASD assessments included gathering developmental history, reviewing prior psychological testing and IEP assessments, administering the ADOS (and cognitive assessments for some children), and integrating information to determine diagnosis.

Results: A total of 62 children were referred for ASD assessment. Children were an average of 10.69 years old (SD = 3.48; range: 5-18 years) and 76% male. They were 42% Latino/Hispanic, 33% Caucasian, 12% African American, 8% Asian/Pacific Islander, and 5% Multiracial. Those referred had an average of 1.79 non-ASD diagnoses (range: 0-5; anxiety, mood, and ADHD disorders were most common) and 48% had two or more comorbid diagnoses. Approximately 70% (n=43) received scores that fell within the ASD or Autism categories on the ADOS. Approximately 56% (n=35) of the sample was assigned an ASD diagnosis by the CMH examiner, primarily Asperger's Disorder (n=10) and PDD-NOS (n=12). Factors associated with receiving an ASD diagnosis, including provider and child clinical characteristics, will be discussed.

Conclusions: The clinical and age characteristics of the children who received an ASD diagnosis after an ASD assessment are consistent with research conducted in similar CMH settings. These data underscore the need for further targeted ASD screening efforts in CMH setting, especially with higher functioning children with comorbid psychiatric conditions. Findings illustrate the feasibility and utility of efforts to implement evidence-based ASD screening and diagnostic practices in CMH settings with relatively minimal extra costs.

116.101 101 Reducing Disparities: Increasing Efficacy of Immigrant Latino Families of Children with ASD. S. Magana*¹, R. R. Paradiso de Sayu² and M. Garcia¹, (1)University of Illinois at Chicago, (2)University of Wisconsin - Madison

Background:

Recent research has found that Latino children in the US are less likely than white children to be diagnosed with an ASD, are more likely to be diagnosed later, and once diagnosed are less likely to receive public and specialty autism related services. Latino children with ASD have also been found to have lower access, utilization and quality of health care than white children with ASD. These findings are exacerbated among Latino children with ASD whose parents are immigrants. Factors that contribute to these barriers include language barriers, lower socio-economic status, and limited information and knowledge about autism and resources. We developed and pilot tested an intervention using Promotoras de Salud (community health workers) to address the educational and informational needs of Latino immigrant parents caring for a child with ASD.

Objectives:

The intervention included 8 home visits conducted by the promotoras who were themselves Spanish-speaking parents of children with ASD. Promotoras were trained in the program's content. We previously presented the quantitative findings of the pilot study and found significant differences between pre and post-tests in family empowerment and caregiver-efficacy. The focus of the present paper is to examine qualitative data to understand the mechanisms by which caregiver-efficacy is improved. Our research questions are: 1) How do the promotoras foster greater caregiver-efficacy in their work with the parents; and 2) What aspects of the program and content are most valuable to parents?

Methods:

We analyzed qualitative responses from two focus groups held after participants completed the program. There were 9 focus group participants in total. Each of the authors reviewed the transcripts independently and identified themes in response to our 2 research questions. We then met to agree upon working definitions of themes and proceeded to recode transcripts independently. When saturation was achieved, the authors

reviewed the coded transcripts and reached agreement.

Results:

Regarding RQ1, participants indicated the *importance of having a role model* who also has a child with ASD. One participant said, "It's beautiful how they (promotoras) are also experiencing the same thing...how they have already had experiences they can share and have been in our shoes." Participants also felt that the promotoras *gave them hope for their child's progress*, "I think they gave us hope for how our children can advance." For RQ2, many participants discussed the value of *knowing they had the right* to ask for services, "now I know I have the right to insist on services my child has the right to receive." Participants also appreciated better *understanding their child's diagnosis*, "It was very useful because the truth is, we didn't know what the definition of autism was very well."

Conclusions:

To address racial/ethnic disparities among children with autism in receiving treatments and services, culturally-based interventions that empower parents are needed. We present data from a pilot study that delivers education to Spanish-speaking immigrant parents in a way that helps them feel empowered and more efficacious in knowing their child's needs and rights and how to advocate for services.

116.102 102 Costs of Care and Canadian Policy Implications: A Lifespan Perspective of Cost of Care for Individuals Living with Autism Spectrum Disorder. J. H. Emery*, C. Dudley¹, D. Nicholas¹ and M. Clarke², (1)University of Calgary, (2)Sinneave Family Foundation

Background:

Care is required for most individuals living with ASD throughout their lifespan. The tasks of care can range from hands on daily living assistance to help managing life skills and finances. Care is provided by a variety of individuals, and much of the care is given by informal caregivers. Day programs, respite services, employment opportunities, and housing all require a range of skilled care providers. Many individuals need help throughout their lifespan but it is often difficult to

find affordable and competent staff to work with people with ASD and to help families. Even where adult services exist staff often do not understand the needs or type of support required and families struggle to find and retain good respite providers. The costs of providing quality care are high. Ensuring the availability of skilled workers may be an issue compounded by challenges of aging informal caregivers, increased longevity of ASD individuals and competing demands for care from an increasing seniors population.

Objectives:

The objectives of this project were to examine the costs of caring for individuals living with ASD, to examine the labour market issues related to availability of care providers and to review provincial government websites for promising Canadian policy or programming to address the high costs of care.

Methods: Caregiver literature was reviewed to locate research pertaining to care tasks and costs across the spectrum. Three case studies were created representing three individuals on the spectrum, care tasks and costs were estimated for each. Key care issues and gaps were identified. These gaps in service were used to focus internet searches for Canadian policies or programs that existed to address the problems.

Results: Each individual across the spectrum receives a range of care throughout their lifespan. Care is provided by a variety of paid workers and informal caregivers. Regardless of who is providing the care, the costs to care can be as high as \$5.5 million over the lifespan of value for caregiver time above the costs of care for a neurotypical individual. Costs of care will reach this level for severe and profound ASD individuals and may decrease for less severe cases. However, costs may be even higher than \$5.5 million if aggressive behaviours are present (2 caregivers required, male providers, and highly trained behavioural staff) and in complex cases (those with co-existing mental health conditions and physical disability).

Conclusions: Standard costs of care previously calculated underestimate the total cost of caregiving time. This project increases awareness

of the high costs of care and broadens the policy discussion needed to begin to address how to care for individuals living with ASD over their lifespan.

116.103 103 Autism and Multidisciplinary Teamwork Through the Scerts Model. P. Molteni*¹ and K. R. Guldberg²,
(1)Università Cattolica del Sacro Cuore, (2)University of Birmingham

Background: An effective educational programme for a child with autism requires the expertise of a team of professionals working together in a careful, coordinated manner, in partnership with parents and family members. Multidisciplinary teamwork is fundamental to understanding and designing a developmental life-long plan for children on the autism spectrum (Prizant et al, 2006). Believing in the importance of multidisciplinary teamwork for children with autism means developing strategies and research that investigate how to implement multidisciplinary work in education.

Objectives: This research examines multidisciplinary teamwork in an English special school through the use of the SCERTS model (Social Communication, Emotional Regulation, Transactional Support). The research analyses the first steps (team design and assessment) of implementing SCERTS by focusing on how professionals can improve the way they work together through the new model. The research questions are: i) How do professionals work together as a team with children on the autism spectrum?; ii) What needs to be done to implement SCERTS?; iii) How can working with children with autism be improved through SCERTS?; iv) What are the positive and challenging aspects of implementing SCERTS?

Methods: This research was designed as an action research collaborative case study using multi-methods approach, thus allowing the researcher to catch the complexity of each single case through a deep detailed analysis of selected aspects. The researcher explored the questions described above with three case studies of children's assessment and their 'Team Around the Child' (22 participants) through focus groups (6), semi-structured interviews (5) and questionnaires (22). The qualitative and quantitative data collected during the research were analysed using Interpretative Phenomenological Analysis (IPA).

Results: The research findings highlight that SCERTS can be a good model for cohering teamwork when working with pupils on the autism spectrum. The results highlight that SCERTS enabled professionals to exchange good daily practice; plan educational work together; and discuss challenges faced in implementing the model. The multi-disciplinary approach realised with the organisation of the TAC was the most innovative element of the SCERTS model and was considered a great improvement in working with children on the autism spectrum as a team. The SCERTS model was efficient in supporting the team in each step of the pupil's educational life plan.

Conclusions: The SCERTS model's flexibility does not cut off the professional's experience and creativity but enriches educational planning by incorporating every point of view on the child as a fundamental resource of information and as equally important.

116.104 104 Three Years of a Specialty Care Programme for Autism Spectrum Disorders. Overview and Clinical Results. C. Llorente*¹, C. Moreno², J. Romo², L. Boada³, M. L. Dorado¹, C. Arango⁴ and M. Parellada⁴, (1)*Child and Adolescent Psychiatry Department, CIBERSAM, Instituto de Investigación Sanitaria Gregorio Marañón, IISGM. Hospital General Universitario Gregorio Marañón.*, (2)*Hospital General Universitario Gregorio Marañón. Instituto de Investigación Sanitaria Gregorio Marañón. IISGM. CIBERSAM, Child and Adolescent Psychiatry Department, Spain*, (3)*Child and Adolescent Psychiatry Department, Hospital General Universitario Gregorio Marañón. Instituto de Investigación Sanitaria Gregorio Marañón. IISGM. CIBERSAM*, (4)*Child and Adolescent Psychiatry Department, Hospital General Universitario Gregorio Marañón. Instituto de Investigación Sanitaria Gregorio Marañón. IISGM. CIBERSAM*

Background: Autism Spectrum Disorders (ASD) individuals have more medical needs, more medical pathology, and greater difficulties in identifying and communicating their symptoms than general population. Medical assistance to ASD subjects is usually poor across contexts. To provide access to high quality medical care for individuals affected with ASD, a comprehensive medical care program was designed and implemented recently in an urban population, in

Madrid (Spain). This program is open to individuals of all ages and serves the whole city's catchment area.

Objectives: 1. Centralizing medical attention and facilitating access to specialized medical care 2. Facilitating differential diagnosis of medical problems, including those leading to behavioural deterioration. 3. To provide access to a Psychiatry Specialized Unit. 4. Improving ASD individuals' health, taking care of daily problems as diet, sleep, dental health. 5. Providing coordination with different medical services to cover medical needs in an organized fashion (reducing waiting times, adjusting spaces with visual sequences and pictograms, performing several procedures in the same day, etc). 6. Enhancing knowledge about ASD among health professionals and promoting specific adaptation of general medical procedures when treating ASD patients.

Methods: Population: ASD individuals of all ages throughout all city's territory (6 million people) Procedure: 1. Setting up a specialised Psychiatry Unit in a Tertiary Hospital for the treatment of ASD patients. 2. Setting up a case management approach. 3. Meetings with the heads of the most demanded specialities. 4. Development of good practice guidelines for the physical environment, medical procedures and diagnostic techniques. 5. Design and application of questionnaires for the evaluation of the effectiveness and satisfaction with the Program 6. Divulcation of the Program among ASD parent associations and educational services.

Results: During the period 1st April 2009 to 30th March 2012, 851 new patients have been attended by this program, 78% children (18

months-17 years) and 22% adults (18 years and older). There have been 3244 follow-up psychiatry visits. In addition, 2733 visits have been organised to other medical specialities and 954 patients have received a medical procedure or a diagnostic technique. The most demanded specialities were Neuropediatrics (N=498), Nutrition (N=394), Ophthalmology (N=334), Gastroenterology-Digestive (N=192), Neurology (N=180), Trauma-Orthopaedics (N=170), Dermatology (N=125), and Estomatology (N=106) The most common procedures and diagnostic techniques were blood test (n=399), electroencephalography (N=145), X-Ray (N=97), echocardiogram (N=86), metabolic and genetic exams (N=83), MRI (N=54) and electrocardiogram (n=51). Preliminary results seem to confirm the presence of more physical pathology in this population.

Conclusions: Persons with ASD display difficulties attending conventional medical settings. A case management approach, with emphasis on information and teaching of professionals, support to patients and families, and coordination between and within medical specialties can cover these needs and improve the medical assistance of ASD population.

116.105 105 School Psychologist Utilization of Evidence-Based Practice for Assessment of Autism Spectrum Disorder. S. Dufek*, L. Schreibman and A. C. Stahmer, *University of California, San Diego*

Background: Although there are many global similarities between children with ASD, the population is extremely heterogeneous. Evaluating a child for ASD is often complicated, as practitioners must evaluate a wide range of behavior to determine where a child falls on the autism spectrum. The recent reported increase in the prevalence of ASD has created a growing demand for cutting-edge research examining how evidence-based practices (EBPs) developed for children with ASD can be effectively disseminated

into community practice to improve diagnostic accuracy. Although consistency and reliability for ASD assessment practice has been established in the research community, it is unclear how ASDs are being assessed in community settings such as schools.

Objectives: This study assessed the benefits of training school psychologists to use evidence-based practices (EBPs) for ASD evaluations in school settings.

Methods: A single-subject, multiple-baseline design across participants was implemented with six school psychologists who collectively assessed 78 children for ASD over the course of the study. After a baseline phase where usual care for assessment of children with ASD was monitored, school psychologists were trained to utilize two standardized ASD assessments considered EBP for ASD evaluation in research settings: the Autism Diagnostic Observation Schedule (ADOS) and the Social Communication Questionnaire (SCQ). Throughout the study, ASD evaluations performed by participating school psychologists were videotaped and their subsequent child evaluation reports were collected in order to assess any effects of ADOS or SCQ training on school psychologist practice.

Results: Results indicate that school psychologists utilize a wide variety of practices when assessing children for ASD in the school setting but do not often use EBPs. School psychologists were not performing ADOS-related tasks during their usual care ASD assessment practice and many ASD-specific symptoms were not mentioned in subsequent child evaluation reports. After a 2-day ADOS Clinical Training, school psychologists administered the ADOS with good fidelity of implementation. Coding of individual ADOS items was challenging for the school psychologists, although overall ADOS classification determinations were typically accurate. Use of the SCQ was somewhat limited after training. Examination of child evaluation reports indicated that the school psychologists captured more ASD-specific behaviors after ADOS and SCQ training.

Conclusions: School psychologists can and will utilize the ADOS, and to a lesser extent the SCQ, to evaluate children for ASD in the school setting with minimal training. Challenges to and

advantages of school psychologist use of EBPs such as the ADOS and SCQ for ASD assessment will be discussed.

116.106 106 Integrating Research, Practice and Policy in ASD. L. White*¹, S. J. Carrington², B. Winn¹, C. Ramsden¹, H. Morgan³ and S. R. Leekam¹, (1)*Cardiff University*, (2)*Wales Autism Research Centre*, (3)*Autism Cymru*

Background: Research in ASD has helped to advance our knowledge about evidence-based methods for identification, diagnosis and intervention in ASD. However, much of the new knowledge emerging from this research is not reaching the people who need it. Many users of autism services, practitioners and policy-makers are not aware of research evidence and how to evaluate it. Likewise, some key issues affecting individuals with autism that are being articulated by government agencies, third-sector organisations and service users are not impacting on research.

Objectives: 1) to facilitate sharing of expert knowledge across areas of research, policy and practice 2) To increase awareness and understanding of evidence-based scientific research in the non-academic community and 3) to promote engagement with users of future research through consultation and participation.

Methods: (1) A web-based electronic forum was developed to promote the sharing of expertise between practitioners and researchers for specific topics (e.g. diagnosis, sensory symptoms). (2) Two 'research aware' resources were designed; a 'research aware leaflet' for parents and a 'research toolkit' for practitioners, each focused on enhancing research knowledge about intervention. (3) Familiarisation resources were designed for potential users of researchers; a booklet and DVD about neuroimaging research.

Results: (1) The web-based electronic forum for practitioners and researchers generated debate and discussion between more than 100 researchers and practitioners, including discussion in advance of two international meetings. (2) Consultation with potential users of the 'research aware' resources identified aspects of research methodology that are not understood by either parents or practitioners. (3) Engagement with users of research through the familiarisation resources resulted in half of them expressing an

interest in participating in future neuroimaging research.

Conclusions: Results of the electronic forum activity helped to identify patterns of user activity that will inform the development of a larger scale online networking area. Further work is needed to increase understanding of research evidence and willingness to incorporate it into decision making in policy and practice. Increasing engagement and participation in research will be accompanied by improved dialogue and two-way communication between researchers and users of ASD research.

116.107 107 Perceived Autonomy Support in Children with Autism Spectrum Disorder. N. M. Shea*¹, J. J. Diehl², K. Tang², M. Van Ness², S. L. Mazur² and M. Millea³, (1)*Syracuse University*, (2)*University of Notre Dame*, (3)*Nielsen NeuroFocus*

Background: Autonomy support is critical in child development; it has been linked to both greater school and friendship outcomes. Little research has been conducted on the benefits of autonomy support for children with autism spectrum disorder (ASD). Traditional therapies for children with ASD focus on using controls and rewards which are at odds with autonomy support.

Objectives: This study had two specific aims: (1) to examine whether greater teacher autonomy support would lead to greater scholastic competence, and to see if this relationship was mediated by self-determination in school in adolescents with ASD, and (2) to examine whether greater parent autonomy support would lead to greater social competence, and to see if this relationship was mediated by self-determination in friendship in adolescents with ASD.

Methods: Participants were 26 adolescents with ASD between the ages of 9-15 years with an average IQ score of 107.73, ranging from 78 to 142. Diagnoses were confirmed using the ADOS, SCQ-Lifetime, and clinical judgment. Participants completed six self-report measures regarding parent and teacher autonomy support, self-determination in school and friendships, and social and academic competence. The Learning Climate Questionnaire (LCQ; Williams & Deci, 1996) was used to assess the adolescent's perceptions of their teacher's autonomy support. The Academic Self-Regulation Questionnaire

(SRQ-A; Ryan & Connel, 1989) was used to assess self-determination in school. The Perceptions of Parents Scale, The Child Scale (POPS; Grolnick et al., 1991) was used to assess adolescent's perceptions of the degree to which their parent were autonomy supportive. The Friendship Self-Regulation Questionnaire (SRQ-F) was used to assess the degree to which the adolescent felt self-determined and autonomous with respect to friendship. Two subscales from the Self-Perceptions Profile for Children (SPPC; Harter, 1985) were used: the scholastic competence (SPPC-SC) and social acceptance (SPPC-SA). The SPPC-SC measured scholastic competence and the SPPC-SA measured social acceptance.

Results: Self-determination in school functioned as a mediator between teacher autonomy support and scholastic competence. Using a 95% confidence interval with 1000 resamples of the data, it was found that the bias corrected and accelerated confidence interval obtained from testing the indirect pathways did not include zero, CI [.01, .12], indicating that the indirect pathway from teacher autonomy support to scholastic competence via self determination was significant. Self-determination in friendship did not function as a mediator between parent autonomy support and social acceptance. Contrary to our predictions, the indirect pathways for maternal autonomy support (CI [-.40, .16]) and for paternal autonomy support (CI [-.31, .33]), were not significant. However, self-determination in friendship (SRQ-F) was strongly correlated with reports of social acceptance (SPPC-SA), $r = .55, p < .01$.

Conclusions: The findings from this study provided initial evidence that autonomy support is beneficial for adolescents with ASD; greater teacher autonomy support lead to greater scholastic competence in adolescents with ASD.

Future research should explore ways to make existing treatments for children with ASD more autonomy supportive or explore the development of new therapies that emphasize autonomy support and the development of self-determination.

116.108 108 Participatory Research Partnerships in Autism Research.
J. Jivraj*¹, A. Newton¹, D. Nicholas² and L. Zwaigenbaum¹,
(1)University of Alberta, (2)University of Calgary

Background:

Participatory research (PR) is an approach that aims to increase the relevance and implementation of health research by involving end-users, those affected by the outcomes of health studies, in addition to academic researchers in developing research. While the importance of involving end-users at all levels of health research is widely recognized, few studies within the field of autism research involve autistic adults as research partners. Recognizing the potential relevance of related populations to understanding the value of PR paradigms in informing autism research, PR partnerships involving people with other neurodevelopmental disorders were also examined.

Objectives:

(1) Identify existing PR partnerships between academic researchers and individuals with autism or other neurodevelopmental disorders; (2) examine the reported impact of these partnerships on quality of research in primary literature; and (3) map out existing studies documenting such partnerships.

Methods:

A scoping review of literature on PR partnerships between academic researchers and individuals with autism or other neurodevelopmental disorders was conducted. A comprehensive search of the literature between January 1950 and September 2012 was completed. Studies were identified through electronic searches of Medline, Embase, CINAHL, PsycINFO, and EBSCO. Grey literature and bibliographies were also searched. Retained studies described research partnerships in which individuals with autism or other neurodevelopmental disorders participated in one or more stages of research development and contained descriptions of the participatory process.

Results:

Of the 754 studies yielded from a librarian-guided literature search, only five described PR partnerships between academic researchers and individuals with autism or other

neurodevelopmental disorders. Four were qualitative studies guided by the participatory action framework, and one employed a mixed-methods design using the Delphi method of consultation. One study examined participatory research partnerships between academic researchers and adults with autism, and four studies examined participatory research partnerships with adults with neurodevelopmental disorders.

The PR partnerships were grouped into two categories: partnerships active during the initial development of the research project (two studies; end-user involvement in setting research questions and identifying research priorities) and partnerships involving end-user involvement throughout the research project (three studies; end-user involvement in conducting study, data analyses, and/or dissemination of research findings). Each study described the benefits of PR partnerships with respect to research quality; these included the addition of the end-user's experiential knowledge, which enhanced the relevance of the research. Common challenges reported in the studies included addressing diverse communication needs and maintaining active end-user participation despite time constraints.

Conclusions:

This scoping review revealed positive impacts of PR research in the field of autism and neurodevelopmental disorders which were consistent with the findings of systematic reviews of PR partnerships in the broader health research literature. However, within the limited number of such PR partnerships, gaps in the reporting of strategies enabling optimal PR partnerships within the autism and neurodevelopmental disorder population were revealed. Further development and assessment of PR partnerships is warranted in autism research.

Core Deficits Program

117 Core Deficits I

117.109 109 Developmental Profiling of Voice Quality in Infants At Risk of Autism. S. Ghai*, K. L. Muench, A. Klin and G. Ramsay, *Marcus Autism Center, Children's Healthcare of Atlanta & Emory University School of Medicine*

Background:

Atypicalities in vocal behavior have been consistently associated with autism since the earliest descriptions of the condition. Many studies analyzing speech development in autism have focused on investigating differences in intonation and rhythm associated specifically with prosodic deficits that seem to be characteristic of ASD. In our previous research, we showed that prosodic deficits, in the form of elevated and more variable fundamental frequency contours, may appear within the first year of life in infants at risk of autism, accompanied by atypical patterns of vocal interaction. However, it is not yet clear whether differences in prosody are specifically linked to deficits in social engagement, as our data suggest, or might instead simply be due to more general problems with motor control seen in ASD. Since fundamental frequency is only one property of the speech signal, characteristics of other voice source parameters might reveal a clearer picture about the origin of speech disorders in autism.

Objectives:

The goal of this study is to analyze developmental profiles of voice quality measures in the first two years of life in infants at risk of autism. By comparing measures that characterize different aspects of glottal function, we test the hypothesis that vocal atypicalities in high-risk infants reflect a core prosodic deficit specific to autism, as opposed to a more general deficit in phonatory function arising from motor impairments comorbid with ASD.

Methods:

As part of an ongoing study, speech data were collected from 4 low-risk infants with no family history of autism and 4 high-risk infants with older siblings already diagnosed with autism. Day-long audio recordings of each child were made with a digital audio recording device (LENA Foundation) sent to participating families by mail and worn by the child for the entire day of the recording. The recording sessions began at 2 months and continued at monthly intervals for 12 months. Non-cry vocalizations for each child were extracted from each recording by hand labeling. Standard measures of voice quality including the fundamental frequency, open quotient, return quotient and speed quotient were estimated on a frame-by-frame basis for all segmented speech

files. Developmental changes in all of our measures were quantified by using Functional Data Analysis to align the resulting densely sampled longitudinal profiles across individuals and derive growth charts of vocal development. Clinical assessments were carried out at 24 months to determine outcome.

Results:

In our high-risk sample, two infants were diagnosed with broader autism phenotype and two had non-autistic language delays; all low-risk infants were found to be typically developing. Voice quality profiles showed that fundamental frequency was elevated and more variable across BAP and LD infants, diverging from TD infants at around 9 months. No significant differences are currently observed in our other measures.

Conclusions:

Our results indicate that atypical vocal behavior in infants at risk of autism begins to develop towards the end of the first year of life, and may present as specific differences in intonational prosody rather than properties reflecting more general problems in phonatory control.

117.110 110 Pupillary Light Reflex Constriction Amplitude's Correlation to Clinical Symptoms. J. H. Miles¹, T. N. Takahashi*¹, C. L. Daluwatte² and G. Yao², (1)*Thompson Center for Autism and Neurodevelopmental Disorders*, (2)*University of Missouri Columbia*

Background: Pupillary light reflex (PLR) provides a non-invasive model system for study of the nervous system in ASD. Pupillary response to a light flash includes a latency period, then pupil constriction and recovery. Daluwatte et al, (2012) found PLR parameters discriminated ASD children from typical developing (TD) controls with 87.7% specificity and 76.4% sensitivity. Four PLR measurements (constriction amplitude (CA), latency, constriction time, redilation time) were calculated to quantify PLR. Though latency was the strongest ASD predictor, each parameter strengthened the association. To determine significance of each parameter and to assess their potential usefulness as ASD biomarkers, we have undertaken an analysis of associations between PLR parameters and ASD symptoms. Constriction amplitude (CA) assesses autonomic function,

since the constriction sphincter is innervated by the parasympathetic system. A small but consistent literature finds that children with autism have lower parasympathetic and higher sympathetic activity. Moreover, children with ASD commonly present with GI, urinary, sensory, sleep disturbances which are to some degree under ANS control. We question whether variation in CA might inform us about systemic ANS dysfunction.

Objectives: Investigate the association between CA and clinical ASD symptoms.

Methods: PLR was measured in 152 children with ASD (age 10.7±3.4 years, 135 males and 17 females) and 107 TD children (age 10.9 ± 2.9 years, 79 males and 28 females). PLR induced by a 100ms green light was measured in light adapted and dark adapted conditions using a two channel binocular apparatus. PLR measurements were calculated to quantify PLR. A parent questionnaire designed to evaluate areas of ANS participation, including GI, GU, fever response, sleep and hyper-sensitivity was completed. From this group, 53 ASD children who had also completed the Simons Simplex Study were selected for preliminary analysis.

Results: CA was in autism range or below for 53%, in normal range for 34% and equivocal for 13%. Using CA as dependent variable, we found low CA correlated significantly with lower IQ (FSIQ & NVIQ; p= 0.02, VIQ: p=0.03). In addition, children with the lowest CA were more than twice as likely to have parents report improvement in core ASD symptoms with fever (40% vs19%). This confirmed findings from our initial PLR subjects (Fan et al., 2009). Systemic symptoms influenced by the ANS (GI, sensory, sweating, salivation, urination, swallowing, sleep disturbances) were not associated with CA. Though not reaching significance the low CA group showed a trend toward further neurologic dysfunction based on higher toe walking and dysmorphology.

Conclusions: PLR CA is a measure of ANS activity. Our data show CA correlates inversely with heart rate, indicating low pupillary CA could be an indicator of systemic ANS dysfunction in ASD. In this small sample none of the clinical symptoms suggestive of ANS dysfunction correlate with CA. We did find children with the smallest CA

had significantly lower IQs suggesting variation in CA may be a marker for general neurologic disruption. Clarification of these results will depend on our ongoing analysis in the entire sample of 152 ASD children and 107 TD children.

117.111 111 A Tool for Setting Therapeutic Goals by the Multidisciplinary Team for the Preschool Age Child with ASD. A. Kotsopoulos^{*1}, A. Georgiou², M. Gyftogianni², K. Gyftogianni², I. Florou², A. Troupou² and M. Sakellari²,
(1)*Technological Institute of Patras*, (2)*EPSYPEA*

Background: The clinical profile of children with ASD varies considerably at the early stages of development. A variety of specific deficits may be observed e.g. feeding difficulties, motor and verbal dyspraxia, sensory integration deficits, perceptual deficits etc, therefore the need for multidisciplinary observation and assessment is necessary for setting realistic therapeutic targets. In 2007 the interdisciplinary team of the Day Centre developed a behavior observation tool (EDALFA) which provides a clinical profile of the child's level of function and detailed targets for intervention.

Objectives: To test the validity of EDALFA in relation to VINELAND questionnaire filled by the parents, and to examine the usefulness of the tool in the clinical application over the years.

Methods: EDALFA consists of a developmental scale based on eight international scales and systematic review of the recent literature. It includes the following observation measures: **motor development** (gross and fine movements), **cognitive development, speech and language development** (comprehension and expression), **psychosocial development** (emotions-social skills), **everyday skills** (feeding, dressing, and toilet training), **play**, and a new one **other** (joined attention, imitation, stereotypes). In every one of those functions, at each age level (1 month to 6 years) skills ranging from 0 to 9 are described, which the typically developing child is expected to master.

Upon admission to the program three therapists (behavior, speech, occupational) observe systematically the child on a sufficient number of sessions and jointly complete the EDALFA protocol, which shows the developmental profile of the child compared to the typically developing child. A diagram of the child's functional profile is

drawn, and the targets (skills not mastered) to be addressed in therapy emerge.

The sample consisted of thirty children (30) (2yrs. to 5yrs 11 months. average: 3yrs 9 months.) diagnosed with ASD (DSM-V). For each one of them the VINELAND questionnaire was filled by the parents and EDALFA was completed by the team. A correlation analysis was made between measures shared by the two assessment tools.

The usefulness of EDALFA was tested using reassessments of the child's progress, which are carried out routinely at regular intervals to set new targets. The profiles of the child over time were compared with his clinical progress in order to find out whether the measures concurred.

Results: The correlation between EDALFA and VINELAND was statistically significant (r ranged from 0,61 to 0,84 in seven measures). The observed changes in the EDALFA profiles over the years of treatment corresponded strongly with the clinical progress of the child. Furthermore, the close cooperation of the different professionals sensitized the therapists to the holistic approach of the child with ASD. The therapeutic targets were shared with the parents and teachers contributing further to the child's progress.

Conclusions: EDALFA in practice showed satisfactory usefulness in identifying non developed skills and setting hierarchical targets for the interdisciplinary team, the parents and teachers.

117.112 112 Gender Differences in ASD Symptoms in Adults with High Functioning Autism Spectrum Disorders. W. T. Brooks*, H. M. Scott, B. A. Benson and M. E. Moran,
Nisonger Center

Background: Autism spectrum disorders (ASD) are diagnosed about four to five times more frequently in males than in females. Consequently, much of the early ASD research focused exclusively on males. Only recently have gender differences in the presentation and characterization of ASD gained momentum in the literature. This burgeoning body of research suggests that gender may affect the presentation of ASD, leading to a "gender-specific" ASD phenotype, in which females present with a different pattern of socio-communicative

impairments and restricted interests and behavior than males.

Objectives: The aim of this project is to examine gender differences in adults with high functioning autism spectrum disorders (HFASD) in self-report and parent-report ASD questionnaires, and in an observational assessment of ASD symptoms, as well as correlations among these different types of ASD measures.

Methods: This project is part of a larger study examining gender differences in ASD symptoms, social relationships, and emotions in adults with HFASD. Data collection is still in process, and it is expected that by the time of the conference in May 2013, there will be data for 60 participants with HFASD, 30 women and 30 men matched on age and verbal IQ. Participants were recruited from several local organizations serving individuals with ASD and their families. Parents of potential participants completed the high-functioning Autism Spectrum Screening Questionnaire (ASSQ), a screening measure for HFASD that was adapted for use with adults in this study, and the ASSQ-GIRL, an addition to the ASSQ recently developed to assess ASD features that may be more applicable to females with ASD. Participants completed the Autism Spectrum Quotient (AQ), a self-report ASD screening measure. Researchers assessed participants with the Autism Diagnostic Observation Schedule-2nd Edition (ADOS-2) and the Wechsler Abbreviated Scale of Intelligence-2nd Edition (WASI-2) to confirm that intellectual disability (ID) was not present. Participants included 20 adults (12 women and 8 men) with a mean age of 26.4 years (SD=5.5 years), who had been diagnosed with an ASD by clinical psychologists, psychiatrists, and other medical professionals, per parent report. Men and women with HFASD did not differ significantly on age, living situation, ethnicity, employment, or WASI-2 verbal comprehension index scores.

Results: There were no significant differences between men and women on ASSQ, AQ, or ADOS total and domain scores. However, women did score higher on the ASSQ-GIRL (mean = 16.3, SD = 6.3) scale than men (mean = 11.3, SD = 5.4), and there was a trend towards significance ($t=1.87, p=.078$) with a large effect size (Cohen's $d=0.86$). ASSQ-GIRL scores and the ADOS-2

communication domain score were significantly negatively correlated ($r = -.54, p= .014$), suggesting that as ASSQ-GIRL scores increased, deficits in communication decreased.

Conclusions: Preliminary results from the study suggest some important gender differences. Women scored higher on the ASSQ-GIRL, and this measure was associated with lower communication deficits on an observational measure of ASD symptoms. These results suggest that the ASSQ-GIRL may add important information to the assessment and characterization of females with HFASD.

117.113 113 Validation of the Korean M-CHAT: Preliminary Data.
H. Seung*¹, S. J. Kim², G. Hong², H. Lee³ and M. Chang⁴,
(1)California State University, (2)Nazarene University,
(3)Yeung Nam University, (4)Seo Kyeong University

Background:

The importance of early identification of children at risk of being diagnosed with autism is critical for better intervention outcomes. Kim et al. (2002) examined validity of Korean Checklist of Autism in Toddlers (CHAT, Baron-Cohen, 1992) in 16-20 month old children. The Modified-Checklist of Autism in Toddlers (M-CHAT, Robbins et al., 2001) is an expansion of the CHAT in the number of items (9 to 23 items) and age range (18 months to 16-30 months). The M-CHAT has demonstrated utility in screening children for autism. However, no study has yet validated whether the Korean version of the M-CHAT identifies Korean children at risk as sensitively as the English M-CHAT.

Objectives:

1) To evaluate the validity of the Korean M-CHAT in unselected children by using the English screening criteria (either fail two or more on the six critical items, or three or more on the 23 total items), 2) to examine the Korean translation by examining response distribution on each item, 3) to examine positive predictive value (number who screened positive/total children screened) and negative predictive value (number who screened negative/total children screened), and 4) to examine if the Korean M-CHAT can be used for children between 16 and 36 months (instead of 16-30 months).

Methods:

Parents of 16-36 month old children were recruited at a Public Health Center where parents brought children for vaccinations, and public/private daycare centers across South Korea. A two page printed copy in Korean (California State University, Fullerton, IRB approved informed consent form and the M-CHAT) was presented to parents.

Results:

The results of this submission are based on a subset of data collected in Chungcheongnam-Do ($n=219$). Seven hundred respondents have completed the Korean M-CHAT since July 2012; data collection will continue with a goal of recruiting 1000 participants. The scoring is well underway using the automatic scoring program that Diana Robins made available. Data coding and analysis will be completed by March, 2013.

Results of current data were 163/219 (74 %) screened negative and 56/219 (26 %) screened positive based on parents' responses using the English screening criteria. A follow-up interview with those who screened positive resulted 1.4% confirmed positive, 13.7% confirmed negative, and 10.5% remained as screen positive (unable to complete follow-up interview for various reasons such as no contact information provided, did not want to speak to the researcher, or cannot reach parent despite multiple attempts).

Most parents followed-up failed on item 11 (Does your child ever seem oversensitive to noise?) and 18 (Does your child make unusual finger movements near his/her face?) on their initial responses.

Conclusions:

The Korean M-CHAT seems to be a good test to screen for a potential diagnosis of autism for children under age three, when used with a follow-up interview for those items failed.

It will be cost effective to train public health professionals (pediatricians, nurses, day care center personnel) on the use of the Korean M-CHAT. Subsequently, they would administer it

during office visits, score it on site, and do a follow-up interview as necessary.

117.114 114 Cross-Cultural Differences in Responses to Sexuality within ASD Across Asian and Australian Cultures. A. Kaur¹ and M. A. Stokes^{*2}, (1)Monash Medical Centre, (2)School of Psychology, Deakin University

Background: Adolescents with Autistic Spectrum Disorder (ASD) have a nascent sexuality that continues to develop, albeit delayed when compared to their typically developing (TD) counterparts. However, this then interacts both with parental and societal expectations. Consequently, it is likely adolescents with ASD may express somewhat different sexual problems depending upon the ambient cultural milieu, in turn revealing something of the importance of culture to the development of sexuality among these persons. Further, the extent to which stability is found across culture would reveal something of the biological contribution of ASD to the disparate sexual development in this group.

Objectives: Thus, to explore the effect of culture upon the nascent sexuality of persons with ASD, we hypothesized that persons with ASD would be reported as having greater problems with sexuality than either other group, regardless of country.

Methods: We examined TD persons ($n=153$), persons with ASD ($n=66$), and persons with Down's syndrome (DS; as a second control; $n=111$) aged between 10 and 20 years of age from three cultures: Australia ($n=129$), India ($n=120$), and Singapore ($n=81$). Using the Sexualised Behavior Scale - 2nd Edition (SBS-II) we examined parental responses concerning their child's Social Contact, Social Insight, Sexual Behavior and the Parents own future concerns.

Results: Significant interactions were found across culture and condition for Social Contact ($p<0.05$, $\eta_p^2=.02$), and after controlling for social contact, for social insight ($p<0.001$, $\eta_p^2=.10$), and Parental Concerns ($p<0.05$, $\eta_p^2=.04$). Problematic sexual behavior was only differentiated by diagnosis ($p<0.001$, $\eta_p^2=.16$), and remained significant even when controlling for social contact and social insight ($p<0.001$, $\eta_p^2=.07$).

Conclusions: These findings reveal that the profound issues that arise in sexual development remain difficult for persons with ASD after controlling for their social and cultural milieu. Thus, culture, while important, is not the cause of sexual problems observed among those with ASD. Therefore, while interventions in this area need to be culturally specific and culturally sensitive, they first need to address basic issues common to all groups examined.

117.115 115 Tackling Teenage in High Functioning-Autism Spectrum Disorder Adolescents (HF-ASD): A Pilot Project in Barcelona. R. Calvo Escalona^{*1}, O. Puig Navarro², C. Amat³, L. Peran³, R. Balcells⁴ and J. Castro-Fornieles¹, (1)*Hospital Clinic of Barcelona*, (2)*SGR 1119*, (3)*Catalonian Asperger's Association*, (4)*Hospital de Mataró*

Background: Adolescence is a transition period of life, especially difficult for Autism Spectrum Disorder (ASD) adolescents, who have scarce social understanding and difficulties to cope with changes. Discrepancies between socio-emotional and physical development arouse driving to frustration and disturbances in socio-emotional behavior (Stokes, 2007; Ballan, 2011). At Yulius Health Institution in The Netherlands, Dutch researchers have developed the Tackling Teenage (TT) Training, a program based on previous psychoeducative and cognitive models (Hellemans, 2007; Sperry and Mesibov, 2006) and aimed to improve psycho-sexual development in ASD adolescents.

Objectives: 1) To adapt the TT program to our environment in collaboration with the Rotterdam research team. 2) To replicate the previous positive results in High-Functioning ASD (HF-ASD) adolescents.

Methods: The TT consists of 18 weekly individual sessions with a trained psychologist. The topics and themes of the TT adapt the psychosexual education and interpersonal abilities to the knowledge and functioning levels of the adolescent. Effects of TT were investigated by comparing the knowledge and skills of the HF-ASD adolescents before (T1) and after the training (T2). Baseline assessment included the ADI-R, WISC-IV or the WAIS-III depending on age, the Social Responsiveness Scale (SRS), the Child Behavior Checklist (CBCL) and the Knowledge Test (KT) about human biology. The SRS, the CBCL and the KT were administered again at T2.

At the moment, 14 adolescents with DSM-IV diagnosis of HF-ASD and with VIQ>80 have been recruited and six have completed the training. All diagnoses were confirmed with ADI-R and clinical consensus of the research team. Ethical board committees of both hospitals have authorized the present study.

Results: Mean age of the recruited sample (n = 14) was 15.36 years (SD 1.6) and included 3 females. The IQ was in the normal range (102.2; SD 13.84). They showed significant level of autistic symptoms, with means of 17.91 (SD 5.24), 14.91 (SD 4.32), 4.36 (3.14) and 1.9 (2.13) for the ADI-R areas. The SRS mean at baseline was 79.92 (SD 28.26). The CBCL mean total score was 60.4 (SD 10.84). They had a mean of 24.39 (SD 7.15) in the KT. No significant differences were found between the recruited sample and participants who have finished the training (n = 6).

The pre-post analysis showed a significant improvement of social communication deficits (t = 4.95, p = 0.004) and a significant improvement of knowledge (t = -3.52, p = 0.010) after intervention. No significant differences were found in the total score of the CBCL (p = 0.436) nor in the internalized or externalized symptoms subscales (p = 0.41). A negative significant correlation was found between increase knowledge after intervention and age (r=-0.77, p=0.036).

Conclusions: These preliminary findings suggest that the TT increases knowledge on sexuality as well as decreases of severity of communication deficits as measured by SRS in HF-ASD adolescents. In this Spanish sample, younger ones seem to improve more.

117.116 116 An Exploratory Factor Analysis On the 3di Supports the Proposed DSM-5 Model. W. De la Marche^{*1}, I. Noens¹, B. Boets¹ and J. Steyaert², (1)*University of Leuven (KU Leuven)*, (2)*Maastricht University Hospital*

Background: In light of the newly proposed DSM-5 criteria, there is a growing interest in the underlying factor structure of autism spectrum disorders (ASD). A number of studies applied confirmatory factor analysis to investigate this structure on the basis of Autism Diagnostic Interview (- Revised) or Developmental, Dimensional and Diagnostic Interview (3di)

domain scores. Yet, these studies are based on a priori theoretical perspectives, because they actively impose a model on the data by (1) using confirmatory factor analysis, and (2) basing the analysis on domain scores which represent DSM-IV-TR diagnostic criteria (operationalized in a number of questions/items).

Objectives: We aimed to explore the factor structure of ASD starting from 3di subscale scores without imposing any a priori theoretical restrictions. Doing this, we want to explore the internal consistency of DSM-domain content and the validity of the two-domain structure proposed in DSM-5.

Methods: The 3di was administered to parents of 275 Dutch speaking participants with ASD (59 girls, 216 boys; age range 4 to 22 years; 16 with intellectual disability, 269 high functioning). Thirty-seven subscales of the 3di were entered in an exploratory principal components factor analysis with varimax rotation: the 36 items used in the original diagnostic algorithm (based on DSM-IV-TR criteria) and one additional item targeting sensory sensitivity (which is proposed as an additional diagnostic criterion for ASD in DSM-5).

Results: Based on the scree rule, a two factor model was proposed. The first factor consists of subscales targeting non-verbal social behavior, sharing, offering comfort, imaginative play with peers, social overtures, conventional gestures, reciprocal conversation and imaginative play on one's own and imitation. The second factor comprises the subscales targeting stereotyped, repetitive or idiosyncratic speech, ritualistic behavior, mannerisms, preoccupation with non-functional aspects of objects or their parts and auditory sensitivity.

Conclusions: This exploratory factor analysis is an empirically driven attempt to capture the underlying phenotypical dimensions of ASD by investigating the coherence between individual 3di subscales. The findings generally support the proposed DSM-5 two domain model: (1) a merging of scales targeting *deficits in social communication and interaction* into one factor, and (2) a pooling of scales targeting *restricted, repetitive patterns of behavior, interests or activities*, including idiosyncratic, stereotyped and

repetitive speech, and some aspects of atypical sensory processing. Contrary to the DSM-5 proposal, our data suggest to incorporate imaginative play and imitation as aspects of the social communication and interaction domain.

117.117 A Sequential-Longitudinal Study On the Origins of Theory of Mind Abilities in Children with ASDs. R. Fadda*¹, M. Parisi¹, R. Fanari¹, D. Rollo², M. Foscoliano³ and G. S. Doneddu³, (1)University of Cagliari, (2)University of Parma, (3)Azienda Ospedaliera Brotzu

Background: Major questions in the field of Theory of Mind concerns its founding factors. Researchers abundantly focused on declarative pointing, mirror self-recognition and symbolic play. However, there is still no agreement among researchers about the mentalistic nature of these abilities (see for example Perner e Ruffman, 2005; Lillard, 1993), and the longitudinal studies which demonstrate clearly the relationship existing among precursors and later mentalistic abilities are still rare, especially in children with Autism Spectrum Disorders (ASDs), who are known to be impoverished in Theory of Mind despite quite intact metarepresentational skills (Baron-Cohen, 1989).

Objectives: This study aimed to investigate the sequential relationship between declarative pointing, mirror-self recognition and symbolic play before 24 months and a later mentalistic abilities, speech about internal states, that emerge between the 26th and 30 month, in children with ASDs in comparison to developmental age-matched controls.

Methods: A sequential-longitudinal study was conducted considering two groups of ASDs children. The first group (n=17; 15M), mean developmental age at T1=16 months (SD=3.95), mean chronological age=44 months (SD=9.85), was assessed longitudinally from 16 to 24 months, every two months. Participants in this group were tested for declarative pointing, mirror self-recognition and symbolic play. The second group (n=12; 9M), mean developmental age at T1=22 months (SD=1.345), mean chronological age=57 months (SD=5.794), was tested longitudinally from 22 to 30 months, every two months. Participants in this group were tested for speech about internal states. The children of the two groups which resulted homogenous at the age of their overlapping (22-24 months) in the

abilities considered were collapsed into an unique longitudinal sample and the sequential correlations between early and later abilities were calculated. The same design was applied to two groups of developmental age-matched Typically Developing controls (TD).

Results: While in the majority of TD children mirror self-recognition was present at 17 months, followed by declarative pointing at 18 months and by symbolic play at 20 months, in children with ASDs all these abilities were lacking except mirror self-recognition, which was very strong at 18 months of developmental age. Speech about internal states was quite lower in both groups at 30 months. However, while in TD there was a correlation respectively between speech about internal states at 30 months and declarative pointing ($r=0,825$; $p<0.05$) and mirror self-recognition ($r=0,917$; $p=0,014$), there were not correlations between early and later Theory of Mind abilities in ASDs.

Conclusions: These results seems to support the hypothesis of a non mentalistic interpretation of the precursors of Theory of Mind (Perner e Ruffman, 2005), which claims that children might learn to predict the behaviour of the other people on the basis of rules learned by previous experiences and therefore they might be successful in some Theory of Mind tasks, like the ones evaluating speech about mental states, without actually engage in a properly mentalising process.

117.118 118 Identifying Unexpected and Inappropriate Words in ASD Language Samples. E. T. Prud'hommeaux*, M. Rouhizadeh, B. Roark and J. van Santen, *Oregon Health & Science University*

Background: Idiosyncratic and atypical language is included in many diagnostic instruments, including the ADOS, ADI-R, and SCQ, as a diagnostic marker for autism spectrum disorder (ASD). Judgments of atypicality, however, rely primarily on impressionistic, real-time evaluation of language at the discourse level, which can lead to poor reliability across examiners and subjects. In this study, we use both manual assessment and automated language analysis of speech transcripts of narratives to identify instances of atypical and inappropriate language at the lexical level. We then use this information to distinguish

children with typical development (TD) from children with ASD.

Objectives: The objectives of this work are the following: (1) to establish that children with ASD use unexpected or inappropriate words in their narratives; (2) to investigate methods of identifying such words automatically and objectively using existing language analysis technology; and (3) to determine whether these automated methods are an adequate substitute for manual analysis for distinguishing children with ASD from their TD peers.

Methods: Participants in this study included 37 children with TD and 21 children with ASD, who were diagnosed via clinical consensus according to the DSM-IV criteria and the established threshold scores on the ADOS and the SCQ. There were no significant between-group differences in age (mean=6.4) or full-scale IQ (mean=114). The Narrative Memory subtest of the NEPSY, in which a child hears a brief story and must retell the story to the examiner, was administered to each child. Each retelling was recorded and then transcribed. Two annotators, blind to diagnosis, identified every word in each retelling transcript that was unexpected or inappropriate given the context of the story. In order to identify such words automatically, we then calculated for each word the *tf-idf* score, which is based on a comparison between the frequency of that word in the child's retelling and the frequency of that word in a large corpus of retellings collected from neurotypical adults. A high *tf-idf* score indicates that a word is very unlikely or unexpected in that particular context.

Results: First, we found that children with ASD do, in fact, produce significantly more manually identified unexpected and inappropriate words in their narrative retellings ($p < 0.05$). Second, the set of words selected as unexpected using the automatic *tf-idf* score corresponds very well with the set of words manually identified as unexpected (precision=84%, recall=53%). Finally, using the set of automatically identified words, we found again that children with ASD produce significantly more unexpected words than children with TD ($p < 0.05$).

Conclusions: These results demonstrate that identifying specific instances of atypical language

at the lexical level can reveal patterns of language use that are characteristic of ASD. The word likelihood score presented here captures these patterns accurately enough to allow for automated analysis of language that can serve as a proxy for manual identification of unexpected words. This work underscores the potential of automated techniques for improving our understanding of the linguistic features associated with ASD.

117.119 The Developmental Profile of Perspective-Taking in Written Story Production by Children with ASD. L. Stirling*, G. Barrington, S. Douglas and K. Delves, *University of Melbourne*

Background:

While numerous studies of the language of children with Autism Spectrum Disorders (ASDs) have included narrative tasks, minimal work has been done on written language. Furthermore, managing shifts of perspective in narrative is a task that might be expected to present particular difficulties to children with ASDs. Yet this aspect of narrative construction has received comparatively little attention. Earlier studies examined lexical items used to report character speech and mental states, but rarely looked beyond the lexical level in evaluating the use of perspectivisation in narrative production.

Objectives:

We investigate written narrative capability in high-functioning children with ASDs attending mainstream schooling, focusing on the kind and complexity of their perspectivisation. Our aim is to investigate whether the developmental profile of narrative and perspectivisation ability in the ASD children is similar or different to that of TD children, and whether the profile shows delay or differential rate of development compared to this group. We measure this feature with a novel analytic tool, and consider this both with respect to a comparison group of TD children from the same school environments, and against a larger baseline study of TD primary school children.

Methods:

A purpose-designed computer-based story elicitation environment was used to collect written story retellings by children at their schools or

homes. The children were read a stimulus story of a culturally familiar type on two consecutive days then given up to 40 minutes to complete the task.

35 participants with ASDs were involved aged 6-13, all of whom had had a team assessment from a recognised child mental health service or autism specialist and were high-functioning with IQ above 70. All attended mainstream primary schools. They were paired with 29 TD children of the same gender, grade and school as ASD participants. A baseline cross-sectional study of 148 TD children across the 7 years of primary schooling was undertaken to collect normative and developmental data, using the same task.

In addition to a range of standard measures of length and linguistic complexity, 'Perspective space' analysis provided an alternative metric for capturing story complexity grounded in the representation of character speech/thought. Both shifts in perspectivisation and whether the speech reported was represented as dialogic or not were coded.

Results:

The baseline TD study showed some measures of narrative complexity including mean number of perspective spaces per story exhibited a strongly incremental linear progression through year levels of primary schooling. Furthermore, there was a significant effect for gender on this parameter.

The stories by ASD children analysed to date suggest differences in kind of perspectivisation used and a developmental profile indicating a slower start and more variance across year levels, but overall a similar developmental progression.

Conclusions:

This study indicates the value of perspective space analysis as a measure of sophistication in narrative production. As TD children move through primary school they become progressively more sophisticated in their management of perspective and interaction representation. We describe the developmental profile of perspective management in stories by ASD children against this background.

117.120 120 Early Vocal Development in Infants At Risk of Autism: Prosodic Development, Social Interaction, and Outcome. K. L. Muench*, S. Ghai, A. Klin and G. Ramsay, *Marcus Autism Center, Children's Healthcare of Atlanta & Emory University School of Medicine*

Background: Although deficits in receptive and expressive prosody are accepted as key symptoms of autism, the origin and the nature of their progression remain elusive. Typically developing infants transition from purely reflexive to more complex intonation patterns as they gain volitional control. An infant's prosody is further shaped by engagement with the social world, particularly in response to the exaggerated prosody of a caregiver attempting to attract infant attention. Prosody thus becomes an important index of social attunement between infant and caregiver as infants respond to and learn from their caregiver's voice. It is possible that specific developmental problems in social interaction and speech displayed by a child with autism at age two may be observable much earlier in atypical development of prosodic exchanges in infancy.

Objectives: The goal of this study is to explore the potential of prospective longitudinal measures of vocal behavior to inform clinical diagnosis by correlating prosodic development in the first two years of life with standard measures used for clinical assessment of autism. We test the hypothesis that abnormal early development of intonational interactions is predictive of later outcome.

Methods: As part of an ongoing pilot project now funded through an NIH Autism Center of Excellence, we recruited 4 low-risk infants with no history of autism and 4 high-risk infants with older siblings diagnosed with autism. We collected high-quality day-long audio recordings of each infant in their home environment at monthly intervals from 2 months onward using a miniature digital audio recording device (LENA Foundation) worn in the child's clothing. We then collected a battery of clinical assessment measures from each child at two years of age. At each time point, we extracted sequences of utterances containing infant-caregiver interactions and calculated three measures of prosodic development: the fundamental frequency contour, utterance duration, and relative timing between utterances. Using Functional Data Analysis to align the resulting densely sampled longitudinal profiles

across individuals, we were able to quantify developmental changes in all of our measures. We were then able to compare differences in developmental trajectories with differences in clinical outcome measures.

Results: Our final sample consisted of 4 typically developing children (TD), 2 children diagnosed with a language delay (LD), and 2 children diagnosed with broader autism phenotype (BAP). Group differences in fundamental frequency contour, utterance duration, and relative timing predicted categorization into TD and non-TD groups as determined by clinicians. Group-level categorizations based on prosodic measures were consistent with categorizations based on the ADOS summary scores. However, prosodic measures were not sufficient on their own to distinguish between LD and BAP subgroups.

Conclusions: Preliminary results suggest that typically developing and developmentally delayed infants may differ according to acoustic measures of atypical prosodic development. However, these vocal measures alone appear insufficient to discriminate between children with language delay and children with broader autism phenotype.

117.121 121 Comparison of Methods for Assessing Receptive Language Knowledge in Minimally Verbal Children and Young Adults with Autism Spectrum Disorders. D. Plesa Skwerer*, S. Siegel, A. A. Harris, S. R. Messier and H. Tager-Flusberg, *Boston University*

Background: Assessing receptive language skills in individuals with autism spectrum disorder (ASD) who fail to acquire functional speech (20-30%) is challenging due to pragmatic, motivational and behavioral problems. Research has often not included these individuals and their actual linguistic knowledge remains poorly characterized. Interest in devising alternative methods for probing comprehension abilities in minimally-verbal (MV) individuals with ASD is growing (Tager-Flusberg & Kasari, 2012), underscoring the need for analyses of the feasibility of these methods and comparisons of their efficacy. We are conducting a multimethod study of different novel assessment measures of receptive language in MV individuals with ASD (ages 7-21) compared to verbal, high functioning (HFA) children with ASD, using eye-movements, touch screen responses, and EEG recordings

alongside standardized testing and parental reports of language comprehension.

Objectives: We aim to evaluate the feasibility of novel experimental methods to measure receptive language in school-age and older MV children with ASD, to compare their efficacy to providing valid data, and to explore individualized approaches to assessment.

Methods: A looking-while-listening paradigm was administered to monitor language-mediated eye-movements as implicit measures of lexical knowledge using a TobiiT-60 eye-tracker. Image-pairs were displayed for 5 seconds and the target word (noun, verb, adjective - matching one image) was played 2.5 seconds after stimulus onset. Trials were distributed over 3 developmentally ordered blocks. Participants completed a similar paradigm on a touch screen device, as well as a standardized test of receptive vocabulary (PPVT-4). Parents reviewed a list of all of the words used as stimuli and indicated which were "understood only" or "understood and produced" by the child. Five MV (Mean age=16.1 years) and 4 HFA participants (Mean age=13.1 years) completed all assessments over 3-4 visits.

Results: Analyses of eye-tracking data suggest that measures of language-mediated visual attention deployment (total duration of fixations and mean fixation count on the target image after auditory stimulus onset) provide evidence of implicit language comprehension in the MV group. The MV participants looked longer and more often at the matching versus the foil in pair ($M=.23$ sec. versus $.16$ sec., $t(3) = 2.9$, $p = .05$ and $M= 1.1$ versus $.63$, $t(3) = 8.2$, $p = .004$, respectively), consistent with the pattern found in typically developing individuals, and replicated in our HFA group. This pattern was found for 4 MV participants, and matched the words parents indicated as understood by their child. Performance on the touch screen device was the most reliable indicator of comprehension for two MV participants (98% and 75% accuracy respectively, when compared to the percentage of trials with increased attention deployment to targets after word-onset, 68% and 32%, respectively, in the looking-while-listening task).

Conclusions: The significance of alternative methods for receptive language assessment in MV

persons using more sensitive measures of comprehension (e.g., attention deployment or motor response) versus relying on compliance with standardized testing will be discussed in light of the findings. We will also discuss the need for individualized testing protocols including possible strategies for designing flexible assessments that provide valid, reliable data for this population.

117.122 122 Marital and Coparenting Quality in Families of Children with Autism Spectrum Disorders (ASDs). A. R. Ly*¹ and W. A. Goldberg², (1)University of Delaware, (2)University of California, Irvine

Background: Because the nature of ASDs profoundly affects the family as a unit, there is a call for research to take a systemic approach to examine the interconnected relationships between parents and their children. Most of the existing research focuses on the mother; there is little information about fathers of children with ASDs and little about the family triad. The current multi-method, multi-source study includes both dyadic and triadic family constructs as reported by and observed for both mothers and fathers of children with ASDs.

Objectives: To determine if the level of ASD symptoms moderates the relationships between marital quality and coparenting with child behaviors

Methods: Participants were 60 families of children diagnosed with ASDs aged 3-7 years ($M = 5.33$; $SD = 1.37$). Mothers and fathers were diverse in terms of ethnicity, education, and income. Parents completed questionnaires and were observed with their child in videotaped play interactions at the family home. Two measures of aspects of marital functioning were used: (1) Marital Adjustment Test (Locke & Wallace, 1959) and (2) the marital conflict subscale of Braiker & Kelley's (1979) Partnership Questionnaire. Two methods were used to assess coparenting: (1) the Coparenting Scale (McHale, 1997) and observer ratings from triadic family play session (McHale et al., 2001). Observed coparenting resulted in three factors: family harmony, hostility-competitiveness, and parenting discrepancy. Children's adaptive and problem behaviors were measured on the Vineland Adaptive Behavior Scales-II (Sparrow, et al., 2005). Negative affect was measured using a subscale of the Children's Behavior Questionnaire-Very Short (Putnam &

Rothbart, 2006). The Social Communication Questionnaire (SCQ; Rutter, et al., 2003), a measure of social-communicative impairment, was tested as a moderator.

Results: For both mothers' and fathers' reports, the relationship between self-reported coparenting and child behavior outcomes is not moderated by the level of child symptoms. Using observed coparenting, the relationship between any of the observed coparenting factors and mothers' reports of child behaviors is not moderated by the level of child symptoms. However, for fathers, the level of ASD symptoms emerged as significant moderators of the relationships between: (1) parenting discrepancy and child adaptive behaviors ($\beta = .24, p < .05$), (2) hostility-competitiveness and child maladaptive behaviors ($\beta = .39, p < .01$), and (3) family harmony and child negative affect ($\beta = .39, p < .05$). For children with low levels of ASD symptoms, greater family harmony and parenting discrepancy are associated with poorer child outcomes; greater hostility-competitiveness is associated with better child outcomes. For children with a high level of symptoms, the opposite findings are found: greater family harmony and parenting discrepancy are associated with better child outcomes; greater hostility-competitiveness is associated with poorer outcomes.

Conclusions: Although many researchers regard family involvement in the intervention process as a crucial (Dawson & Osterling, 1997), little empirical data have been available about fathers and the family system. Our results reinforce the importance and complexity of including fathers and contribute to the literature on the conceptual and empirical distinctions between marital quality and coparenting.

117.123 Reliabilities and Validities of the Chinese Mandarin Version of the Social Communication Questionnaire (SCQ) From a Population-Based Study in Taiwan. P. C. Tsai*¹, L. C. Lee¹, R. Harrington¹, I. T. Li², C. L. Chang³ and F. W. Lung⁴, (1)Johns Hopkins Bloomberg School of Public Health, (2)Calo Hospital, (3)Kaohsiung Armed Forces General Hospital, (4)Taipei City Hospital

Background: Many people live with ASD without being diagnosed. Such under-diagnosis is especially prominent for underserved populations. While providing clinical assessments to each individual in a population is not practical, multi-

stage case identification that involves screening followed by clinical evaluation is a feasible way to identify ASD, especially for populations without complete autism or autism-related services registries. Screeners that aim to identify individuals at high risk for ASD are vital for multi-stage case identification. The SCQ rates autism-related behaviors and was used as a screener to identify children at high risk for ASD. The SCQ was developed and widely used for studies in Western countries. In order to adapt the tool for use in international settings outside of Western countries required provision of its strong reliabilities and validities.

Objectives: To establish reliabilities and validities of the Chinese Mandarin Version of the SCQ, and to present distributions of the SCQ total score and three sub-domain scores by child sex and SES factors.

Methods: A population-based epidemiologic study of autism in children aged 6-8 involving a multi-stage case identification design was conducted in PingTung, Taiwan from 2008-2010. The SCQ was translated and back-translated into traditional Chinese Mandarin and pilot tested before its use in this population. Data from a total of 2279 primary caregivers (60.0% mothers, 17.5% fathers, 22.5% grandparents and others) who completed the screener on their child (1083 boys and 1156 girls) are included in this analysis. The three sub-domains of SCQ are: Reciprocal Social Interaction, Communication, and Restricted/ Repetitive/ Stereotyped Behaviors. Reliability was assessed using Cronbach's alpha (internal consistency). Factor analyses in full sample, and sample with total score ≥ 15 (a high risk for ASD) were performed separately to assess the difference in SCQ-measured behaviors in full sample and in ASD high-risk sample.

Results: The reliability alphas are 0.67, 0.80, 0.81, and 0.83 for Communication, Reciprocal Social Interaction, Restricted/ Repetitive/ Stereotyped Behaviors, and full scale, respectively. Factors of SCQ measured behaviors are different for the full sample and the ASD high-risk sample (i.e. SCQ ≥ 15).

Conclusions: Overall, the internal consistency (measured by alpha) of the SCQ full scale and three domains are good, but the Communication

domain is fair. Results from the factor analyses reveal different factors in the sub-sample with high ASD risk ($SCQ \geq 15$) and in the full sample. The mean scores of the caregiver reported autism-related behaviors in boys are higher than in girls when the SCQ scores are examined as continuous; however, the difference is not substantial. Caregiver reported autism-related behaviors are associated with respondents' characteristics in this large scale population-based study in Taiwan. Fathers reported more behavioral issues in their child than did mothers and other caregivers; and lower education levels were associated with reports of clinically concerning autism-related behaviors.

117.124 124 Measuring Language Competence in Children with ASD and Average Intelligence. C. R. Newsom* and B. Corbett, *Vanderbilt University*

Background: Social communication impairments are a defining feature of ASD; however, children with ASD show heterogeneity in language competence. Standardized measures of communication may not capture subtle impairments shown by children with HFA. We rely on these measures to diagnose language impairment, determine eligibility for services, define participant or diagnostic groups, and measure response to intervention.

Objectives: This study aims to identify measures of language competence that are sensitive to the milder but significant language impairments characteristic of children with HFA. We will explore whether direct and parent report measures of language competency correlate with social language use in a naturalistic playground setting.

Methods: Thirty-three boys with autism and 29 TD controls participated in a study that included direct assessment of cognitive development and language competency, parent report, and a playground interaction captured by video. Participants ranged from age 8 to 12, and were matched for age (M 9.73, SD 1.48). Intelligence was estimated using the WASI, with a mean IQ of 108.2 (SD 24.5) for the ASD group and a 120.4 (SD 13.8) for the TD group. All participants had a FSIQ of ≥ 80 . The ASD group diagnosis was made by a clinical psychologist with expertise in ASD and confirmed with an ADOS. Video data from playground interactions will be coded for frequency of Verbal Initiation, Verbal Rejection, and Verbal Bouts (duration and number of verbal exchanges). Participants completed the Clinical

Evaluation of Language Fundamentals - Fourth Edition (CELF - 4) subtests Concepts and Following Directions (CFD), Recalling Sentences (RS), and Formulated Sentences (FS). Parent estimates of child language facility included the Adaptive Behavior Assessment System-Second Edition (ABAS-II), the Social Communication Questionnaire (SCQ), and the Social Responsiveness Scale (SRS).

Results: Controlling for IQ, a significant multivariate main effect for group was observed for the CELF-4, $F(3, 56) = 5.36, p = .003$, partial eta squared = .223. Between group differences were statistically significant for the CELF-4 CFD $F(1) = 15.12, p < .001$ and FS $F(1) = 4.77, p = 0.03$, with children with ASD performing more poorly. Across groups, the Concept and Following Directions scale is moderately correlated with ABAS Communication ($r = .42, p = .001$) the SRS Social Communication Scale ($r = -.41, p = .001$) and the SCQ ($r = -.39, p = .002$). The Formulating Sentences scale is also moderately correlated with ABAS Communication ($r = .42, p = .001$), SRS Social Communication ($r = -.32, p = .01$), and SCQ ($r = -.36, p = .004$).

Conclusions: Group differences emerged between TD and HFA children on measures of ability to follow auditory instructions and verbally formulate sentences, with children with ASD showing greater signs of impairment. Parent report of communication skills in social and daily living settings were also significantly different across groups and moderately correlated with direct child assessment. Additional analysis of language data collected in naturalistic playground setting will speak to which type of measure, parent or child measures, are better predictors of language competence in a naturalistic playground situation.

117.125 125 Non-Linear Analyses of Speech and Prosody in Asperger's Syndrome. R. Fusaroli*¹, D. Bang² and E. Weed³, (1)*Aarhus University*, (2)*Magdalen College*, (3)*Aarhus University Hospital*

Background:

It is widely acknowledged that people on the ASD spectrum behave atypically in the way they modulate aspects of speech and voice, including pitch, fluency, and voice quality. ASD speech has been described at times as "odd", "mechanical", or "monotone". However, it has proven difficult to quantify and explain this oddness of speech pattern.

Objectives:

In this project, we quantify how the speech patterns of people with Asperger's Syndrome (AS) differ from that of matched controls. To do so, we employed both traditional measures (pitch range and standard deviation, pause duration, and so on) and 2) non-linear techniques measuring the structure (regularity and complexity) of verbal, prosodic and fluency behaviour. Our aims were (1) to achieve a more fine-grained understanding of the speech patterns in AS than has previously been achieved using traditional, linear measures of prosody and fluency, and (2) to employ the results in a supervised machine-learning process (discriminant function) to classify speech production as either belonging to the control or the AS group, based solely on acoustic features.

Methods:

Our analysis was based on previously-acquired narratives of the Frith-Happé triangles by 10 people with AS and 10 matched controls, with 8 narratives per subject. Transcripts were time-coded, and pitch (F0), as well as speech-pause sequences were extracted. Each of these time-series was then used to calculate mean, standard deviation, Shannon entropy, noise distribution (Hurst exponent) and recurrence quantification measures. The results were employed to train a supervised machine-learning algorithm to classify the descriptions as belonging either to the AS or the control group, using a repeated leave-one-out method of cross-validation.

Results:

Overall, we found that the AS group tended to have shorter utterances ($p < 0.05$, $t(18) = 2.70$, effect size = 0.29) and longer pauses ($p < 0.05$, $t(18) = -2.24$, effect size = 0.22). The AS group was also characterized by a higher microscale regularity of prosody and fluency: higher Shannon entropy (fluency: $p < 0.001$, $t(18) = 6.80$, effect size = 0.72; prosody: $p < 0.001$, $t(18) = 9.74$, effect size = 0.85), stronger correlation of neighbouring datapoints in prosody (fluency Hurst exponent: $p < 0.01$, $t(18) = 3.11$, effect size = 0.43) and higher repetition of short sequences of pitch (Recurrence Rate: $p < 0.001$, $t(18) = 9.62$, effect size = 0.83), and speech/pause patterns (Recurrence Rate:

$p < 0.01$, $t(18) = -3.11$, effect size = 0.35). Finally, transcripts in the AS group showed higher regularity, e.g. with stereotyped ways of starting the narratives ($p < 0.001$, $t(18) = 12.61$, effect size = 0.90). These features enable us to automatically classify speech production as either belonging to the control or the AS group with 78.9% accuracy.

Conclusions:

The study points toward the usefulness of non-linear time series analyses techniques in picking out the subtle differences that characterize the unusual voice characteristics of people with AS. It also points to interesting parallelisms between AS patients' speech patterns and repetitiveness in their motor behaviour. Future work includes further validation of the approach, as well as more detailed investigation of the relation between speech patterns and other symptoms.

117.126 126 Is Early Joint Attention Associated with School-Age Pragmatic Language Among Children with ASD, Infant Siblings of Children with Autism and Low-Risk Controls?. K. Gillespie-Lynch*, A. Khalulyan, M. Del Rosario, B. McCarthy, L. Gomez, M. Sigman and T. Hutman, *University of California, Los Angeles*

Background:

Are longitudinal associations between joint attention and structural language (systems of meaning such as syntax or the lexicon; Mundy & Gomes, 1998; Sigman & Ruskin, 1999) attributable to social or representational mechanisms? Reduced joint attention is a core symptom of ASD early in development (Sigman & Ruskin, 1999). While structural language is not always impaired in ASD, atypical pragmatic language (socially appropriate use of language) is characteristic of ASD (Bishop & Baird, 2001; Kjelgaard & Tager-Flusberg, 2001) and the Broader Autism Phenotype (BAP; Bishop et al., 2006; Losh and Piven, 2007). Both joint attention and pragmatic language may arise from social knowledge. Alternatively, rather than emerging from social understanding, the parallel and distributed processing (PDP) model suggests that joint attention emerges from increasing ability to represent triadic relations (Mundy and Jarrold; 2010).

Objectives:

The primary aim of this study was to examine longitudinal relations between joint attention at 18 months and aspects of language that are primarily social (pragmatic language) or primarily representational (structural language) 6 years later in order to evaluate evidence in favor of the social-cognitive (Tomasello, 1995) or the PDP (Mundy & Jarrold, 2010) model of joint attention. A secondary aim was to determine if communicative difficulties were apparent among siblings who did not develop autism.

Methods:

We examined longitudinal relations between joint attention at 18 months and pragmatic and structural language approximately 6 years later among children with ASD ($n = 11$), siblings of children with ASD who did not develop autism ($n = 30$), and low-risk controls ($n = 20$). Initiation and response to joint attention (IJA and RJA) were assessed with the Early Social Communication Scales (Mundy et al., 2003). A parent-report measure of pragmatic language, the Children's Communication Checklist-2 (CCC-2), was used (Bishop, 2003b). Structural language was assessed with both the CCC-2 and the Clinical Evaluation of Language Fundamentals-4 (CELF-4; Semel et al., 2003).

Results:

IJA, but not RJA, was associated with structural ($r(9) = .769, p = .006$), but not pragmatic, language on the CCC-2 among participants with ASD. IJA ($r(8) = .667, p = .031$), but not RJA, was associated with receptive, but not expressive, language on the CELF-4 for children with ASD. No relations between joint attention and language measures were observed for high- and low-risk children without ASD. Children with ASD exhibited reduced RJA ($p = .002$), pragmatic language ($p = .008$), expressive ($p = .024$) and receptive ($p = .001$) language. High-risk participants without ASD did not differ from low-risk participants.

Conclusions:

Despite literature linking joint attention and pragmatic language concurrently among children

with ASD (Loveland & Landry, 1986), relations between joint attention and both parent-report and observational measures of structural, but *not* pragmatic, language were observed. No evidence of BAP related communicative difficulties was apparent. This study, perhaps the first infant sibling study to assess school-age outcomes in ASD, provides support for the PDP theory of joint attention by demonstrating that commonly observed longitudinal associations between joint attention and later language may arise from representational rather than social aspects of both.

117.127 127 Phonological Delay or Phonological Impairment in Autism: An Intergroup Comparison. S. Ferré^{*1}, C. dos Santos¹ and F. Bonnet-Brilhault², (1)Université François Rabelais de Tours; Unité "Imagerie et Cerveau" Inserm UMR 930, CNRS ERL 3106; Tours, France, (2)UMR Inserm U930

Background: Studies (Bartak et al., 1975; Cantwell et al., 1978) investigating language, cognition, and behavior in children with Autistic Spectrum Disorder (ASD) and children with Specific Language Impairment (SLI) suggested clear differences between these two groups. In fact, Kjelgaard et al. (2001) showed that among the children with autism there was significant heterogeneity in language skills. Some children with autism had normal language skills and others had language skills significantly below age expectations. The actual debate opposes the view that children with ASD have the same language profile as children with SLI against the view that these children present a delayed acquisition rather than a deviancy as some studies suggested it (Tager-Flusberg, 1981; Tager-Flusberg et al., 1990).

Objectives: The objective is to determine whether one aspect of atypical language development in ASD (i.e. phonology) is only characterized by a simple delay in development or if it also shows some similarity with structural language impairment found in children with SLI. For this objective, we recruited a group of English-speaking children that were acquiring French as a second language. This group has, indeed, a delayed acquisition of French compared to typical French speaking children.

Methods: We compared productions of three groups of children at a word repetition task

recorded at one year gap (T1 and T2): 28 children with SLI aged 6;5 to 12;11 (mean 9;6), 17 children with ASD aged 6;4 to 12;9 (mean 8;9) and 26 children who have English as first language and French as second language aged 6;4 to 12;7 (mean 9;6). We use the standardized word repetition task of the BILO-3C (Khomsji, 2007). This test includes words of various lengths and different level of phonological complexity.

Results: Overall performances on the word repetition test show that children with SLI have significantly lower scores compared to children with ASD and L2 children (respectively, mean SD: -7.1; -5.1; -2.6). Correlations between word phonological structures and word productions show that children with pathology have difficulties with structural complexity whereas L2 children are mainly influenced by word length. The analysis of vowel production shows that vowels are not problematic for any of these children. However, consonants, and especially clusters, are a source of difficulty for children with ASD and with SLI. Children with ASD show phonological difficulties not linked with their prosodic impairment. Patterns of errors are similar in children with pathology with a preference in using substitution and elision of phonemes. L2 children show a clear preference for elision. They also tend to omit entire syllables instead of isolated phonemes, possibly due to the different stress system found in these two languages.

Conclusions: To conclude, we can say that L2 children are not really affected by structural complexity but rather by a mismatch between French and English prosody. Children with pathology are influenced by complexity rather than prosody. Differences with children with ASD and SLI are mainly seen in the amount of errors, but not in patterns of errors.

117.128 128 Childhood Autism: Comparison Between Impressions of Parents and Educators. D. Satterfield*¹, S. Kang¹, C. Lepage², H. Deering¹ and N. Ladjahasan¹, (1)*Iowa State University*, (2)*Sutter Neuroscience Institute*

Background: The literature indicates that children with ASD experience significant differences in communication, socialization, and behavior as compared to typically developing peers. There is also evidence to suggest that intervention strategies can help children with ASD improve skills in these critical areas. However, the

perceived importance of specific skills in these areas may differ between parents and educators.

In an effort to clarify and address these discrepancies, a series of 5-focus groups were conducted to identify the main deficits in social skills, communication skills, and behavioral skills that negatively impact a child with autism spectrum disorders (ASD) as identified by parents and educators. Parents and educators were also asked to identify the relative importance that they place on social or peer relationships for children with ASD, the situations or contexts that best facilitate socialization, communication, and behavior for children with ASD, and what technologies are most effect to facilitate improved communication, socialization and behavior.

Objectives: There are three main objectives. 1) Identify the communication skills, social skills and behavioral skills that most negatively impact children with ASD as identified by parents and educators. 2) Identify the importance of social and peer relationships as perceived by parents and educators. 3) Identify what situations and technologies best facilitate socialization in children with ASD as identified by parents and educators.

Methods: Full approval was obtained from the ISU IRB. Consent for participation was obtained from each participant. Parents (n=5) and educators (n=5) who work directly with children with ASD in focus groups were asked to respond to questions from a research tool designed to illicit information regarding communication, socialization, behavior and technology. This data was coded to identify patterns in perspectives between these two groups. From this data a mixed-method survey tool was developed. A second set of parents (n=20) and educators (n=20) were asked to complete this survey. Numerical and qualitative data was formulated and reviewed based on the response patterns.

Results: Demographic data including number of males and females, age range, ethnic background, survey results, and discussion of response patterns. Preliminary results from the pilot n=5 groups of parents and educators suggests meaningful discrepancies of their impressions of children with autism.

Conclusions: Patterns in response data between parents and educators in the n=20 groups will be discussed with regard to communication, socialization and behavior skills as well as the perceived negative impacts. Additional discussion includes perceptions of the most effective situations and technologies with respect to improving communication, socialization and behavior skills. Future research will focus on developing those methods of technology, educating treatment teams, and incorporating greater number of high-quality opportunities into daily activity. Level of impairment will be considered as well.

117.129 129 Initial Validation of the Social Communication Checklist. A. Wainer* and B. Ingersoll, *Michigan State University*

Background:

There is a significant need to develop valid and reliable social communication assessment tools for young children with autism spectrum disorders (ASD). The Social Communication Checklist (SCC) is a new measure designed to provide an assessment of social communication skills, including social engagement, language, social imitation, and play, in young children with ASD. The SCC was developed to aid in intervention planning and goal setting, and to provide a measure of social communication intervention outcome.

Objectives:

The objective of the current study was to validate the SCC by exploring the psychometric properties of the measure. In particular, this study sought to explore the internal consistency, test-retest reliability, inter-rater reliability, and construct validity of the SCC.

Methods:

Parents, teachers, and therapists of young children with ASD and related social communication delays completed the SCC, at least one time point, as part of several different intervention studies. Internal consistency, inter-rater reliability, and construct validity, were assessed using data that was collected as part of a study intake assessment battery. Test-retest

reliability was calculated using data from the intake battery, as well as from a post-intervention assessment battery administered several months later.

Results:

The SCC demonstrated good to excellent internal consistency across both parent and teacher/therapist reports. Bivariate correlations revealed moderate to strong associations between parent and teacher/therapist reports across SCC scales and well as for SCC total scores. Bivariate correlations also indicated strong to moderate test-retest reliability for parent and teacher/therapist reports. Follow up t-tests revealed significant differences between time 1 and time 2 parent and teacher/therapist reports suggesting that this instrument is also sensitive to changes in social communication skills over a short period of time (i.e., 3-4 months). Finally, the SCC scales and total score demonstrated strong negative associations with the Social Responsiveness Scale (SRS), suggesting that greater social communication skills as measured by the SCC are related to less autistic symptomatology.

Conclusions:

This initial exploration of the psychometric properties of the SCC suggests that it performs well as an assessment of social communication skills in young children with ASD. Moreover, it appears to be sensitive to changes in core social communication skills over a relatively brief period of time. Thus, results from this study provide initial evidence for the validity of the measure and suggest that it may be a useful social communication assessment tool to use with young children with ASD.

117.130 130 Distinctive Autism Diagnostic Profiles of Latino Children in Puerto Rico. N. Linares-Orama*, *University of Puerto Rico*

Background: There is scarce information about Latino children with autism that can be used in the clinical diagnosis process for this population, particularly those residing in the USA and Puerto Rico. Latinos with autism are the largest group of children in the USA minority population, and clinicians are seeking to differentiate individuals

with autism validly from those of typical development. The DSM-V emphasis on social-communication will require autism diagnosticians to distinguish communication interactions between these groups in order to assure that children with authentic disabilities are those enrolled in clinical and special education programs. This investigation aimed at identifying which observable behaviors can be used in the differential diagnosis process.

Objectives: Our objectives were: 1) to identify social & communication skills that distinguish between severe and moderate autism; 2) to identify social-communication skills that distinguish between mild autism and typical development; and 3) to recommend simplified algorithms for autism diagnosis in the population of USA and Puerto Rico Latino children.

Methods: The method consisted of an IRB-approved record-review investigation of 260 children seen at our Autism Diagnostic Clinic. We analyzed gender, DSM-IV traits, social skills, communication profiles, CARS scores, and diagnostic impressions for this sample. Based on this analysis we conducted statistical calculations to describe the traits that assist in the above-distinctions and provide arguments for a simplified algorithm that can be used validly with the population of Latino children with suspected autism.

Results: Data from the investigation indicates that most children with autism were males, with social interaction disorders as the most frequent DSM-IV trait, followed by repetitive behaviors and, finally, communication impairments, 42.40% were diagnosed with autism and the rest had other developmental disabilities and no-disorders. The most distinguishing CARS characteristics between severe and moderate autism dealt with emphatic behaviors and pragmatic functions. Other distinctive features included message conveyance, detailed story telling, and sustained attention. High-functioning autism represented 15.70%, moderate autism was 15.70%, and low autism was 22.80%.

Conclusions: Our findings revealed that three CARS items are the most distinguishing items for an autism diagnosis, i.e., relationships with other persons (item #1), imitation (#2), and non-verbal

communication (#12). These items need to be used in improved diagnostic protocols that are culturally and linguistically appropriate for the population of Latino children with autism-risk.

117.131 131 Signaling of Non-Comprehension by Boys with Idiopathic Autism, Fragile X Syndrome and Autism, and Typical Development. J. Hornickel*¹, M. Losh¹, G. Martin², S. McGrath² and G. R. Durante², (1)*Northwestern University*, (2)*University of North Carolina at Chapel Hill*

Background: An important component of discourse is to signal to a speaker when you do not comprehend their message. Abbeduto and colleagues (1997, 2008) found that children with intellectual disability (resulting from Down syndrome or fragile X syndrome) make fewer signals of non-comprehension than mental age matched typically-developing peers when presented with inadequate information from the examiner. What is unknown is whether children with autism, known to have deficits in pragmatic language (Tager-Flusberg, 1999), show similar non-comprehension signaling as children with fragile X syndrome or if non-comprehension deficits are largely driven by intellectual disability.

Objectives: We sought to determine if and how children with idiopathic autism signal non-comprehension and whether their signaling techniques differ from children with fragile X syndrome with autism and from typically-developing peers.

Methods: We assessed signals of non-comprehension in boys with idiopathic autism (n = 25), fragile X syndrome with autism (n = 46), and typical development (n = 39), ages 3-17. Following procedures of Abbeduto and colleagues (2008), children were asked to complete a picture matching task by following the directions of an examiner, which contained the appropriate level of detail or incomplete details, including new vocabulary, erroneous information, and not enough information. The proportion of signals of non-comprehension out of possible items was calculated for each condition. All children also completed an appropriate module of the Autism Diagnostic Observational Scale (ADOS) and assessments of theory of mind.

Results: When covarying for receptive language and non-verbal mental ages, we replicated

previous results that boys with fragile X syndrome with autism had fewer signals of non-comprehension than their typically-developing peers across conditions with incomplete information ($t_{83} = 4.467, p < 0.001$). The boys with idiopathic autism did not differ from their typically-developing peers and made significantly more signals of non-comprehension than the boys in the fragile X group ($t_{69} = 4.105, p < 0.001$). ADOS severity scores and theory of mind performance were correlated with proportion of non-comprehension signaling ($r = -0.286, p < 0.01$; $r = 0.286, p < 0.01$, respectively), with greater severity and weaker theory of mind linked to less frequent signaling of non-comprehension, but these correlations were driven by group differences on the measures.

Conclusions: The present results suggest that the pragmatic language deficits associated with autism do not convey additional impairments in non-comprehension signaling as children with idiopathic autism did not differ from typically-developing peers. While autism severity and theory of mind did predict non-comprehension signaling, the relationships were driven by group differences on the measures and were not present within groups. This suggests that previous reports of impairments in non-comprehension signaling by children with fragile X syndrome are not due to overlap in pragmatic deficits with autism, but to another component of the disorder.

References

Abbeduto L, Murphy MM, Kover ST, Giles ND, Karadottir S, et al. (2008). *Am J Ment Retard*, 113(3): 214-230.

Abbeduto L, Short-Meyerson K, Benson G, & Dolish J (1997). *JSLHR*, 40:20-32.

Tager-Flusberg H (1999). *Int Rev Psychiatry*, 11(4): 325-334.

117.132 132 Acoustic Measurements of Prosodic Information in Toddlers with Autism Spectrum Disorders. N. Brosh*¹, J. F. Santos², T. H. Falk³, L. Zwaigenbaum⁴, S. E. Bryson⁵, W. Roberts⁶, I. M. Smith⁵, P. Szatmari⁷ and J. A. Brian⁸,
(1)*Holland Bloorview Kids Rehab Hospital University of Toronto*, (2)*Institut National de la Recherche Scientifique (INRS-EMT), University of Quebec*, (3)*Institut National de la*

Recherche Scientifique (INRS-EMT) University of Quebec, (4)*University of Alberta*, (5)*Dalhousie/IWK Health Centre*, (6)*University of Toronto*, (7)*Offord Centre for Child Studies & McMaster University*, (8)*Holland Bloorview/ Sick Kids*

Background: Disordered prosody (modulation of speech to clarify meaning) has long been considered a hallmark of Autism Spectrum Disorders (ASD; Kanner 1943), and atypical intonation has recently been recognized as an important diagnostic ASD marker (Gotham 2007). Prosodic characterization of children with ASD is an under-researched area, particularly for very young and pre-verbal children, although studies suggest vocal atypicality may represent an early appearing symptom of ASD (Sheinkopf et al 2000). Studies have traditionally evaluated prosody by subjective perceptual analysis (McCann & Peppe 2003). Few studies have utilized objective computerized acoustic voice analysis to measure prosodic elements in children with ASD (e.g., Diehl 2009, Green & Tobin 2009, Oller 2010). No acoustic studies to date have focused on toddlers with ASD, when early diagnosis is often still a challenge.

Objectives: To measure and quantify parameters of intonation, volume and vocal quality using computerized acoustic voice analysis, in toddlers with ASD in comparison to non-ASD controls.

Methods: : Data were derived from the ongoing longitudinal prospective Canadian "Infant Sibling Study" (see Zwaigenbaum et al. 2012). Participants were 23 younger siblings of probands with ASD, followed throughout infancy and independently diagnosed with ASD at age 3 years using the Autism Diagnostic Observation Schedule (ADOS) and Autism Diagnostic Interview – Revised (ADI-R), and an age-matched comparison group (n=20) with no family history of ASD and confirmed as not having ASD at age 3 years. All the toddlers' vocalizations were extracted from video-recorded ADOS assessments conducted at 18 months of age. Vocalizations were converted to audio, de-identified, and digitalized. Non-overlapped segments were acoustically analyzed, using the VoiceSauce MATLAB toolbox optimized for children's speech. A total of 26 acoustic parameters were extracted, related to intonation (pitch), maturity of speech (first formant frequencies and amplitudes), volume (energy) and measures of vocal quality such as voice breathiness, harshness/creakiness (harmonics,

spectral tilt and cepstral peak prominence). Variations on these parameters between groups have been widely used to identify speech disorders. ADOS intonation scores were also compared between groups.

Results: We compared mean, standard deviation (std) and range for the acoustic parameters and found significant between-group differences for 11 parameters, including volume (mean, std, and range), pitch (range) and nine other parameters of vocal quality, using family-wise error rate corrections (p-value range: 0.0001-0.045). Five parameters, the most robust of which was volume, remained significant when subjected to formal Bonferroni correction (critical $p = .05/26 = .0019$). For volume, the mean and range values were more than twice as large for the ASD group ($p=0.0005$). We found no between-group differences for length of ADOS assessment or total duration of analyzed vocalizations, but found a significant group difference for clinician-rated intonation score ($p=.002$); in all cases, values were higher for the ASD group.

Conclusions: We identified and characterized, using objective acoustic measures, early-appearing vocal differences in toddlers later diagnosed with ASD. These findings may contribute to efforts aimed at early detection. Future plans include evaluation at earlier ages (9 and 12 months) and associations between acoustic variables and clinical ratings of intonation.

117.133 133 The Development of the Multidimensional Social Competence Scale (MSCS): A Standardized Measure of Social Competence in Autism Spectrum Disorders. J. Yager and G. Iarocci*, *Simon Fraser University*

Background: Despite the fact that all individuals with ASD meet the social impairment diagnostic criteria outlined in the DSM-IV-TR, they do not all present with the same social difficulties. The variability in the expression and severity of social competence is particularly evident among the group of individuals with "high functioning" ASD who appear to have difficulty applying their average to above average intelligence in a social context. There is a striking paucity of empirical research investigating individual differences in social functioning among individuals with high functioning ASD as well as the implications of these differences on long-term outcomes. It is

possible that more detailed investigations of social competence within ASD have been impeded by the lack of standardized measures available to assess the nature and severity of social impairment.

Objectives: The current study aimed to develop and evaluate a parent rating scale capable of assessing individual differences in social competence (i.e., social strengths and weaknesses) among adolescents with high functioning ASD.

Methods: The newly developed Multidimensional Social Competence Scale (MSCS) was administered via an online survey to the primary caregivers of 183 adolescents (135 ASD, 48 TD). The ADI-R was used to confirm ASD diagnoses. The Social Responsiveness Scale (SRS) was also administered to caregivers in order to evaluate convergent validity of the MSCS.

Results: Results from confirmatory factor analyses supported the hypothesized multidimensional factor structure of the scale. Seven relatively distinct domains of social competence were identified including Social Motivation, Social Inferencing, Demonstrating Empathic Concern, Social Knowledge, Verbal Conversation Skills, Nonverbal Sending Skills, and Emotion Regulation. Psychometric evidence provided preliminary support for the reliability and validity of the scale and included indices of internal consistency, convergent validity, discriminant validity, criterion-related validity, and known groups validity.

Conclusions: The development of the MSCS was informed by a combination of theory-driven and empirical (i.e., data-driven) approaches to test construction. Preliminary evidence suggests that the MSCS is a psychometrically sound parent rating scale that is capable of providing a differentiated assessment of social competence in adolescents with high functioning ASD. Although additional studies are warranted to replicate the results and further document psychometric properties, the MSCS holds promise as a tool that will find many uses in both research and clinical settings. In particular, it is hoped that the scale may offer a means of parsing heterogeneity in ASD by identifying meaningful profiles or patterns of social competence.

117.135 135 Refining the Pittsburgh Inference Test (PIT): A New Measure of Discourse Processing in Individuals with High-Functioning Autism. K. E. Bodner*¹, N. J. Minshe² and D. L. Williams³, (1)University of Missouri, (2)University of Pittsburgh, (3)Duquesne University

Background: Discourse processing is integral to appropriate communication and social interactions, which are known to be impaired in individuals with an autism spectrum disorder (ASD; APA, 2000). Previous tests used to assess discourse processing in ASD are either too simple to assess older, high functioning individuals or are not appropriate for North American populations. The Pittsburgh Inference Test (PIT) was developed as a measure of discourse processing that is sensitive enough to capture the challenges of verbal, older adolescents and adults with high functioning autism (HFA), especially in ascertaining emotion states. However, further evaluation of the PIT is necessary to confirm and extend original findings.

Objectives: The objective of the current study was to further refine the PIT using a larger and more diverse sample.

Methods: The PIT consists of 30 short stories about typical life situations that require inferences about events. Stories are followed by a verbal question that elicits a verbal response. The PIT is comprised of two types of questions that generate responses that: describe physical relationships only or describe physical, mental or emotional inferences (ToM). Responses for each story are scored as correct or incorrect and then categorized as a physical or ToM response. ToM responses are further categorized by: emotion-ToM or other-ToM responses. The PIT and Test of Language Competence-Expanded (TLC-E) were administered to a sample of 86 individuals with HFA (mean=20.6 years) and 65 typically developing (TD) individuals (mean=22.6 years) between the ages of 10-45 years, group-matched for age and IQ [FSIQ, VIQ, & PIQ, $t(149) < 1.82$, $p > .07$]. Autism diagnosis was determined with the ADOS, ADI, and clinical impression. All participants attained FSIQ's > 85 .

Results: After accounting for age and FSIQ, hierarchical regressions confirmed our original findings that individuals with HFA performed worse on the PIT in comparison to TD participants

overall [$t(147) = 4.5$, $pr^2 = .12$, $p < .01$], particularly in ascertaining physical and emotional states [$t(147) > 3.0$, $pr^2 > .06$, $p < .01$]. Other-ToM inference making abilities remained intact [$t(147) = .50$, $pr^2 = .002$, $p = .62$]. Post hoc analyses revealed that only individuals with HFA tended to improve with age in the number of correct [$t(144) = 1.9$, $pr^2 = .03$, $p = .05$] and other-ToM responses [$t(144) = 2.1$, $pr^2 = .03$, $p = .04$]. However, no age-related improvements were noted in physical or emotion-ToM responses [$t(144) < .85$, $pr^2 < .002$, $p > .39$]. Confirming our previous findings, significantly moderate to strong correlations were evident between PIT (excluding physical responses) and TLC-E (subtest 1, 2, and 3) performance ($r = .350 - .722$, $p < .001$), indicating they assess similar underlying constructs of inference abilities. Significant negative correlations were evident for individuals with HFA between ADOS Total score and performance on the PIT, excluding physical responses (r range = $-.562$ to $-.424$, $p < .01$).

Conclusions: The current study confirmed and extended previous findings, which further highlight the usefulness of the PIT as a measure of discourse processing in individuals with HFA.

117.136 136 Construction and Validation of the Early Social Communicative Behavior Questionnaire. M. E. Buruma* and E. M. Blijd-Hoogewys, *Lentis*

Background:

In recent years, there has been an increasing interest in the diagnosis of Autism Spectrum Disorders (ASD) in infants (children younger than 3 years). Research has shown that well-trained clinicians can diagnose ASD reliably in children from 18-24 months on. However, the diagnosis of this age group is complex. First, because the presentation of ASD symptoms can be substantially different than that of an older child with ASD. Second, because the distinction between typical development - which does show a lot of variation at this age - and atypical developmental is difficult. Third, because some characteristics of ASD (such as less social responsiveness, delayed development of language, and repetitive behaviors) also may occur in other developmental disorders and syndromes.

Once diagnosed, early intervention is considered important for infants with ASD, since it may lead to better short- and long-term outcomes. Such programs focus mainly on fostering early social communication, especially joint attention and symbolic play. In order to measure the effect of early intervention programs, there is a need for an instrument that can measure the level of this social communicative functioning. Such an instrument could also be used in diagnostics, since early social communicative problems, including joint attention problems, are one of the most distinctive features in infants with ASD.

Objectives:

The objective of this study was to develop a questionnaire that can be easily used to measure early social communicative behavior in infants in a reliable and valid way.

Methods:

The items for the Early Social Communicative Behavior Questionnaire (ESCBQ) are based on 1) extensive research of literature on both typical and atypical development of early social communicative behavior in infants, 2) existing (international) instruments concerning this topic, and 3) clinical expertise with young children with ASD. There are 108 dichotomous questions formulated: concerning the first year of life, eye contact, social interest, reaction to name, emotions, attachment, sharing pleasure, taking turns, looking, following gaze, following a pointing finger, pointing, showing, giving, playing, interaction games, imitation, gestures, and language.

It takes 20 minutes to fill in the questionnaire. In order to explore the psychometric properties of the ESCBQ, 1200 parents of typically developing children aged 0-6 years filled in the questionnaire.

Results:

The total score of the ESCBQ shows a steady increase with age, with a plateau at 30 months. The internal consistency, based on inter-item reliability, is good (Cronbach's $\alpha = .97$). Also the test-retest reliability (second measurement

after 1 week) is good ($N=43$, Wilcoxon Signed Rank test, $M1=93.19$ vs. $M2=95.63$, $r=.91$, $p=.001$). A Principal component analysis conveyed four factor scores, with the first factor 'pretending and language' explaining 31% of the variance. The other three factors concern pointing, attention shifting and following gaze. These four factors coincide with what is expected from literature. A Mokken scale analysis reveals five scales (ScaleH=.39-.94, 4 scales $>.55$; $Rho=.51-.99$). Further analyses are underway.

Conclusions:

The ESCBQ is a new test with good psychometric properties.

117.137 137 Primary Data On Using Sensors to Analyze Motor Aspects of Gesture Behavior in Children with Autistic Spectrum Disorders. L. Sparaci*¹, D. Formica², F. Lasorsa¹, L. Ricci², P. Venuti³ and O. Capirci¹, (1)*National Research Council of Italy (CNR)*, (2)*Università Campus Bio-Medico*, (3)*University of Trento*

Background: Within our motor repertoire gestures are specific motor acts proving to be very relevant from children's first encounters with communicative contexts. Numerous studies indicate the presence of different impairments in gesture behaviour in children with autistic spectrum disorders (ASD) and highlight how these may play an important role in communication and social interaction deficits present in ASD. However, to date, analyses of gestures produced by children with ASD have relied heavily on traditional video annotation systems. The absence of different measurement tools has overshadowed the importance of analysing motor repertoires exploited by children with ASD during gesture behaviour and prevented comparisons between action and gesture production.

Objectives: In this study we report primary results from the broader TOUM (The Other Understanding in Movement) project. The project aims to develop a novel wearable sensorized platform for the analysis of motor parameters exploited during gestural behaviour in children with ASD and to assess the platform's effectiveness alongside traditional annotation tools. This pilot study evaluates both motor (e.g. limb velocity, orientation, etc.) and formal (e.g. hand shape, palm orientation, etc.) parameters collected using respectively sensors and traditional annotation

systems, during actions and gestures produced by children with ASD and matched typically developing (TD) controls.

Methods: A total of 10 children participated to this pilot study: 5 children with ASD (chronological age 7.2; IQ 90.3) and 5 TD controls (chronological age 6.11; IQ 105.2), matched on chronological and mental age, evaluated using Leiter International Performance Scale Revised. Motor abilities were evaluated using Movement ABC, while linguistic level was evaluated using the Peabody Picture Vocabulary Test and the Boston Naming Test. Children observed a set of short video-clips of an adult performing either actions with objects (e.g. the adult grasps a glass to drink) or corresponding transitive gestures (e.g. the adult raises his hand to the mouth as if drinking) and asked to imitate the observed action/gesture while their movements were measured with the aid of wearable wireless sensors. Children's behaviour during action/gesture production was also videotaped for later coding using traditional annotation systems (i.e. ELAN) and to provide independent measures of action/gesture expressive clarity.

Results: All children were able to imitate the observed actions and to produce at least some gesture types. However closer analysis of both action sequences and gesture behavior of children with ASD showed specifically altered motor patterns, in comparison to children with TD. The different motor parameters exploited by the ASD group had a relevant effect on the quality of performed actions and of produced gestures, altering their expressive clarity. Furthermore, integrating data collected relying on the sensorized platform and using traditional annotation systems allowed to parse out the relevance of motor vs. formal parameters in evaluating gesture performance.

Conclusions: Initial data seem to indicate the possibility of employing novel measurement tools, originally dedicated to motor behavior, to measure gesture production in children with ASD. This new portable and ecological platform in fact allows to capture atypical action/gesture motor patterns, which influence non-verbal behavior and communicative capacities in children with ASD.

117.138 138 Validity of a Brief Joint Attention Scale Based On Items From the SCQ and SRS. S. Novotny*¹, P. C. Mundy², M. Solomon³, W. Jarrold⁴, N. McIntyre⁵, L. Swain¹, N. V. Hatt² and M. Gwaltney⁶, (1)University of California, Davis, (2)University of California at Davis, (3)Department of Psychiatry, MIND Institute, Imaging Research Center, (4)UC Davis, (5)U.C. Davis, (6)University of California Davis, Learning & Mind Sciences

Background: Joint Attention deficits are a hallmark of the social-communication symptoms of Autism Spectrum Disorders (ASD). Because of its central role in the neurodevelopmental disturbance of ASD, it is important to develop brief and accurate measures of Joint Attention (JA) to facilitate research on the genetics, broad phenotype and early identification of this disorder (Mundy, Sullivan, & Mastergeorge, 2009). Recent efforts in this regard has led to the development of a 5-item behavioral observation measure of JA for early identification in a large sample of toddlers (Nygren, Sandberg, Gillstedt, Ekeroth, Arvidsson, & Gillberg, 2012), and a study of genetics using a JA factor isolated from the Autism Diagnostic Interview-Revised (Liu, et al., 2011).

Objectives: The goal of this study was to determine if a valid, brief and theoretically grounded JA scale could be derived from parent reports of ASD symptomatology on the Social Communication Scale (SCQ; Rutter, Bailey, Berument, Lord, & Pickles, 2003) and the Social Responsiveness Scale (SRS; Constantino, et al., 2003). These scales were chosen because they are readily available to researchers and can be used efficiently in large scale genetic and epidemiological studies.

Methods: Participants included 51 typically developing children ($M = 11.88$ years, $SD = 2.47$) and 34 children with a community diagnosis of ASD ($M = 11.85$ years, $SD = 2.52$). All participants had an IQ greater than 75 on the Wechsler Abbreviated Scale of Intelligence (WASI, Wechsler, 1999), with a mean Full Scale IQ of 108.03 (16.58) and 113.91 (14.84) for the ASD and TD samples, respectively. Parents of the participants completed the SRS and the SCQ. Items addressing JA were selected from both questionnaires to comprise a JA scale. Joint attention items were selected on the basis that they assessed the tendency to engage in behaviors that involved adopting a common point

of view or point of reference, either visual or mental, with another person. Seventeen items were selected from the SCQ and SRS and an iterative process of item elimination, based on item-to-item covariance, yielded an 11-item scale (7 SCQ and 4 SRS) that had optimal face validity and psychometric properties.

Results: The SCQ-SRS JA scale had acceptable internal consistency ($\alpha = .836$). A principal components factor analysis indicated that the factor structure of the scale reflected 3 domains: Eye Contact & Social Cognition (ECSC); Joint Visual Attention (JVA); and Social-Communication Gestures (SCG). Discriminant function analysis revealed that the first two factors distinguished higher function children with autism from controls ($N = 85$) with 88.2% sensitivity and 90.2% specificity. The JVA factor was also significantly correlated with social orienting to peripheral peer avatars in a virtual reality social-attention public speaking task ($r = -.383, p < .05$ and $r = -.408, p < .05$).

Conclusions: The results of this study indicate that a valid and useful brief JA parent report measure may be obtained from the SCQ and SRS. These data suggest that additional research and development of a SCQ-SRS JA scale is warranted in studies of larger samples.

117.139 139 The Developmental Check-in (DCI): A New Visual Autism Screening Tool. Y. Janvier^{*1}, J. Harris¹ and D. S. Mandell², (1)*Children's Specialized Hospital*, (2)*Perelman School of Medicine at the University of Pennsylvania*

Background: Racial, ethnic and income disparities in early and accurate diagnosis of autism spectrum disorders may be due, at least in part, to the lack of accuracy in these populations of commonly used autism screening tools. Our prior work has shown that poor and ethnic minority parents of young children had poor knowledge of normal development, misinterpreted behaviors that are considered red flags for autism, and had difficulty reading and understanding items on the Modified Checklist for Autism in Toddlers (M-CHAT) and Social Communication Questionnaire. Based on these findings and with input from focus groups conducted within the underserved communities, we developed a new tool to identify young children with autism, the Developmental Check-In (DCI). The DCI is primarily pictorial and has minimal literacy demands, which reduces

literacy, comprehension, cultural, and language-based barriers that may be inherent in traditional screen instruments.

Objectives: to assess the accuracy of a pictorial screening measure, the Developmental Check-In, developed for a low literacy population .

Methods: The Developmental Check-In (DCI), Screening Test for Autism in Toddlers (STAT) which is a level 2 screening instrument, and M-CHAT were administered to 130 children ages 12-48 months referred to outpatient centers for developmental screening/evaluation. Screening was facilitated by an Advanced Practice Nurse, who also made a clinical diagnosis based on DSM IV criteria.

Results: Of the 130 children, 90 children were screened using all 3 tools, 18 were screened using the DCI and STAT only, 14 were screened using the DCI and M-CHAT only, and 8 received DCI only. ROC analysis revealed no difference between the DCI and the M-CHAT.

Conclusions: The DCI, a pictorial autism screening measure was developed for a low literacy population and was first tested in a literate population, finding no difference between it and the M-CHAT. This suggests it has reasonable psychometrics. Tests in a low literacy group are forthcoming. Since the DCI is pictorial and has reduced literacy demands, it may have utility across cultures and thus may help reduce barriers to accessing early diagnosis

:

117.140 140 Predictors of High and Low Language Skills in Young Children On the Autism Spectrum. S. Ellis-Weismer*, S. T. Kover and H. Sindberg, *University of Wisconsin-Madison*

Background: A primary goal of behavioral research on autism spectrum disorder (ASD) has been to identify predictors of language outcomes (Paul, Chawarska, Cicchetti, & Volkmar, 2008). Variability in language skills among children with ASD is considerable, with some children remaining nonverbal throughout childhood and others attaining age-appropriate language ability. Findings have been mixed with respect to the roles of nonverbal cognition, joint attention,

socioeconomic status (SES), socialization skills, and autism severity for language growth (Bopp & Mirenda, 2011; Paul et al., 2008; Thurm et al., 2007).

Objectives: The purpose of the current study was to further characterize the range of variability in language skills in young children with ASD by identifying factors at approximately 2½ years of age that serve as predictors of language outcomes (i.e., high or low language ability) at 5½ years of age.

Methods: Participants ($n = 103$) were drawn from a longitudinal investigation of language development in toddlers with ASD. Best estimate clinical ASD diagnoses were based in part on the Autism Diagnostic Observation Schedule (ADOS) or Toddler Module (ADOS-T). Initial assessments at approximately 2½ years of age yielded nonverbal cognition scores (Bayley-III cognitive composite), response to and initiation of joint attention (Early Social Communication Scales), SES (years of maternal education), socialization skills (Vineland Socialization standard scores), and autism severity (calibrated ADOS scores). These child and environmental characteristics were considered as predictors in discriminant function analyses between participants with high and low language ability. Participants with high and low language ability were those with Preschool Language Scale-4 (PLS-4) total standard scores that fell within the highest or lowest 15% of the sample of the 103 children at 5½ years of age. Children with high language ability ($n = 15$; PLS-4 standard score $M = 120.93$; $SD = 5.55$) and children with low language ability ($n = 16$; PLS-4 standard score $M = 50.25$; $SD = 1.00$) did not differ in age, $p = .674$. All participants with low language ability were minimally verbal (i.e., scored 3 or 8 on the ADOS item for Overall Level of Non-Echoed Language, indicating fewer than 5 spoken words).

Results: Discriminant functions were limited to three predictors due to sample size. The best 3-predictor model included nonverbal cognition, SES, and response to joint attention and correctly classified 92.3% of valid cases ($n = 14$ high language; $n = 12$ low language): 85.7% of high language cases and 100% of low language cases. Nonverbal cognition alone correctly classified

85.7% of cases: 92.3% for low language and 80.0% for high language.

Conclusions: Early nonverbal cognition is a critical predictor of language outcome; however, the ability to respond to others' bids for attention and environmental factors, such as SES, also discriminated between high and low language ability. These findings have implications for predicting childhood outcomes for individuals with ASD and for identifying potential targets for intervention.

117.141 141 Understanding the Relationship Between Empathy and Social Responsiveness in Young Adults with Autism Spectrum Disorders. E. Javanfar^{*1}, D. Janulaitis², J. Hopkins¹, S. Bates³ and E. Laugeson⁴, (1)UCLA PEERS Clinic, (2)The Help Group - UCLA Autism Research Alliance, (3)UCLA PEERS Program, (4)UCLA Semel Institute for Neuroscience & Human Behavior

Background: Empathy is the capacity to understand and experience the emotional states of others, and is an essential part of social functioning. Previous research indicates that individuals with Autism Spectrum Disorders (ASD) are lacking in empathy and theory of mind, the ability to recognize and understand the thoughts, feelings, and internal states of others (Baron-Cohen & Wheelwright, 2004). Individuals with ASD also demonstrate impairment in social responsiveness (SRS; Constantino & Gruber, 2005), often resulting in the lack of behavioral repertoire necessary to interact with others according to social convention. While the relationship between empathy and social functioning has been examined extensively in the child and adolescent literature, less is known about the relationship between empathic social understanding and social responsiveness in young adults with ASD; thus, limiting our developmental understanding of these constructs.

Objectives: The present study seeks to examine the relationship between self-reported empathy and caregiver-reported social responsiveness in young adults with ASD. It is hypothesized that young adult self-reported empathic social understanding would be correlated with caregiver-reported social responsiveness in young adults with ASD.

Methods: Participants included 39 young adults between 18-27 years of age ($M=20.5$, $SD=2.20$)

presenting for social skills treatment through the UCLA PEERS[®] for Young Adults intervention. In order to understand the relationship between empathy and social responsiveness, baseline assessments of young adult self-perceived empathy were measured using the Empathy Quotient (EQ; Baron-Cohen and Wheelwright, 2004), while caregiver-reported perceptions of young adult social responsiveness were measured using the Social Responsiveness Scale (SRS; Constantino, 2005). To examine the relationship between empathic social understanding and social responsiveness, baseline scores of the Social Skills Subscale of the EQ were correlated with both the Total Score and Subscale Scores of the SRS using Pearson correlations.

Results: Preliminary results reveal that greater impairment on the SRS Social Communication Subscale is significantly correlated with less empathic social understanding on the EQ Social Skills Subscale ($p < .05$). In addition, greater impairments on the SRS Total Score and Social Motivation Subscale are associated with less empathic social understanding on the EQ Social Skills Subscale at a trend level ($p < .10$).

Conclusions: Preliminary findings suggest a strong relationship between empathic social understanding and social responsiveness in young adults with ASD. In particular, deficient social communication abilities appear to be associated with diminished empathy. While the relationship between empathy and social functioning has been examined extensively among children and adolescents, the present study is only one of a few investigating this relationship among young adults with ASD.

117.142 142 Facial Emotion Recognition and Visual Search Strategies of Children with High Functioning Autism and Asperger Syndrome. D. Leung^{*1}, T. Falkmer¹, M. Falkmer¹ and A. Ordqvist², (1)*Curtin University*, (2)*Linköping University*

Background: Poor emotion recognition impacts on a person's ability to self-regulate, and relate to and interact with others; thus, restricting their occupational engagement and social participation. For example, issues with recognising emotions in children and adolescents have been linked with difficulties in managing the social and academic demands of the school environment. Adults with high functioning autism (HFA) and Asperger

syndrome (AS) are often less able to identify facially expressed emotions, and tend to rely less on information from the eye area and attend more often to the mouth when recognising emotions. However, results regarding emotion recognition abilities in children with HFA/AS remain equivocal.

Objectives: The objective was to add to the current knowledge base regarding emotion recognition in people with HFA/AS across the lifespan, by comparing the emotion recognition ability and visual search strategies of children with HFA/AS, aged 8 – 12 years, with that of matched controls.

Methods: The emotion recognition ability and visual search strategies of 26 children with HFA/AS, aged 8 – 12 years, and their matched controls were compared. An eye tracker measured the number of fixations and fixation durations as participants were shown 12 pairs of slides, which displayed photos of faces expressing one of three basic emotional expressions – anger, happiness or surprise. The first slide of each pair showed a face broken up into puzzle pieces. The eyes in half of the puzzle piece slides were bisected, while those in the remaining half were whole. The second slide showed three alternative faces, expressing each of the aforementioned emotions. Participants identified which of the alternative faces was expressing the same emotion shown in the preceding puzzle piece slide.

Results: No differences between the participant groups were found for either emotion recognition ability or number of fixations. Fixation durations were longer in the group with HFA/AS than the controls.

Conclusions: Both groups fixated more often on the eyes and performed better when the eyes were whole, suggesting that both children with HFA/AS and controls consider the eyes to be the most important source of information during emotion recognition. Longer fixation durations indicate that while children with HFA/AS may be able to accurately recognise emotions, they find the task more demanding.

117.143 143 The Female Adaptive Behavior Profile in Asperger Syndrome or High Functioning Autism. I. A. Cox¹, M. A.

Stokes*¹, J. A. McGillivray¹, J. Manjiviona² and T. Attwood³,
(1)Deakin University, (2)Private Practice, (3)The Asperger,s
clinic, Brisbane, Australia

Background: Boys are found to be much more likely than girls to be diagnosed with autism. This ratio ranges from 4:1 to 10:1, depending upon the exact diagnostic categorizations used. Despite over 50 years of research, the reasons for a disparate gender ratio remain unclear, but most disconcertingly, differences in clinical presentation have been little characterized. We examined adaptive behavioral differences in boys and girls, controlling for cognitive differences.

Objectives: We hypothesized that males and females would differ in adaptive behavior.

Methods: We compared 24 typically developing (TD) children (12 to 18 years) to 24 children diagnosed with Asperger Syndrome or High Functioning Autism (AS/HFA) with equal numbers in each gender on the Vineland Adaptive Behavior Scale – second edition (VABS-II, parent rating).

Results: We found significant group differences in adaptive functioning on the domains of socialization, daily living, and adaptive behavior. Using a mixed model MANOVA, and controlling for age and full scale IQ, a significant effect was noted for the interaction of gender and diagnosis ($F_{(1, 42)}=5.0, p<.05, \eta_p^2=.11$), and for the main effect of diagnosis ($F_{(1, 44)}=54.8, p<.001, \eta_p^2=.55$), but not gender.

Conclusions: These results suggest males and females differ in their clinical presentation. Further, they suggest implications for clinical assessment, suggesting girls may not be as apparent as boys in presentation of Autism.

117.144 144 Pragmatic Language Characteristics of Adolescents with Autism and Their Siblings. A. L. Hogan-Brown* and M. Losh, *Northwestern University*

Background: Pragmatic language impairment is a core feature of autism spectrum disorder (ASD), even in individuals with normal structural language and intelligence. Subtler pragmatic language differences have been observed in parents of children with ASD, suggesting that this domain is part of the Broad Autism Phenotype (BAP). However, few studies have measured pragmatic language in unaffected siblings of

children with ASD, nor have they investigated correlations in pragmatic language abilities between probands (i.e., individuals with ASD) and their siblings.

Objectives: To compare pragmatic language behaviors in probands, their siblings, and typically-developing control subjects during semi-naturalistic conversational interactions.

Methods: To date, 41 high-functioning probands ($M = 13.40$ years, $SD = 3.65$), 26 siblings ($M = 13.09$ years, $SD = 3.02$) and 3 control subjects ($M = 15.39$ years, $SD = 1.46$) have been included in this study (with additional control testing currently underway). The Pragmatic Rating Scale for School-Age Children (Landa, 2011) was used to code videos of the Autism Diagnostic Observation Schedule (Lord, 2000). This 33-item measure assesses pragmatic language abilities and associated social-communicative characteristics (e.g., suprasegmental characteristics, nonverbal behaviors). Item scores range from 0 (normal) to 2 (atypical), with higher scores indicating poorer pragmatic abilities. Six subscale scores and a total score are calculated by summing item scores.

Results: Groups differed significantly on the total score ($F(2, 67) = 23.27, p < .001$) and all subscales ($F_s > 7.51, p_s < .01$) except for diversity of speech acts ($p > .05$). Post-hoc comparisons indicated that the ASD group demonstrated poorer pragmatic abilities than the sibling group on presupposition, discourse management, speech and language behaviors, and nonverbal communication, and they differed from both siblings and controls on suprasegmental speech characteristics and the total score. Siblings scored higher than controls on four subscales and the total score (mean difference range: 0.21 – 2.60), but no significant group differences were observed. It is suspected that the differences between the control group and the ASD and sibling groups did not reach significance because of the low number controls subjects. Several correlations emerged between probands and their siblings. Siblings' scores on the presupposition subscale were correlated with probands' discourse management scores ($r = .50, p < .05$), and were marginally correlated with proband total score ($r = .43, p < .10$). Suprasegmental speech characteristics in siblings were correlated with

probands' scores on the discourse management and suprasegmental subscales ($r_s > .52$, $p_s < .05$), and the probands' total score ($r = .49$, $p < .05$). Siblings' total score was also marginally correlated with probands' discourse management abilities ($r = .42$, $p < .10$). Interestingly, when proband scores were examined in relationship to those of an unrelated child from the sibling group, matched on age and gender to their own sibling, no significant correlations emerged, supporting familial relationships in pragmatic language ability.

Conclusions: These results provide additional evidence of pervasive pragmatic language impairments in high-functioning adolescents with ASD, and also support the possibility that pragmatic language characteristics stem from shared genetic and/or environmental factors.

117.145 145 Autism Spectrum Disorder: Potential Presence in Online College Community. D. Satterfield*¹, C. Lepage² and N. Ladjahasan¹, (1)*Iowa State University*, (2)*Sutter Neuroscience Institute*

Background: The literature has shown that many people with an ASD have repetitive behaviors as well as difficulty with transitions and problem solving. These atypical patterns are only a part of the constellation of functional impairments seen in ASD. These behaviors however, significantly impact adaptive skills, educational success, and professional development.

Engineering and Human Computer Interaction (HCI) students at Iowa State University completed an online course addressing human-computer interface technology for persons with supportive needs. During this course, students were provided with information about autism and some of these students indicated suspicion for a self-diagnosis of social skills deficits. Following this interesting pattern, the 42 adult students who recently completed the course were asked to participate in the current project.

For the current project, each of the 42-students were asked retrospectively (after the conclusion of the course) to complete the Ritvo Autism-Asperger's Diagnostic Scale Revised (RAADS-R) as well as a questionnaire inquiring about their course experience. RAADS-R results divided the students into two groups: those scoring at or

above research-validated threshold and those scoring below.

Objectives: The objectives of this study were 1) to investigate the potential presence of patterns seen on the autism spectrum in students completing an online university-level design course and 2) review the feedback of two groups: those meeting or exceeding ASD cut-off scores on the RAADS-R and those who did not.

Methods: Full approval was obtained from the ISU IRB. Consent for participation was obtained from each student participant. Students ($n=42$) who recently completed the online design course were asked to complete the RAADS-R, a research validated tool designed to clarify the possible presence of an autism spectrum disorder in adults. Two clusters were established: 1) Meets or exceeds RAADS-R threshold, and 2) below RAADS-R threshold. Course feedback was evaluated from the perspective of the two groups. Numerical data was formulated and reviewed based on the response patterns.

Results: At the time of this submission, data collection is underway and scheduled to be completed in December 2012. Demographic data is to be determined, but includes number of males and females, age range, ethnic background, RAADS-R results, and discussion of response patterns.

Conclusions: Hypothesis include 1) Based on RAADS-R responses, an emerging trend toward previously unidentified patterns suggestive of autism-like patterns in the online university-student population and 2) Patterns of perseveration on course minutiae in these different populations. Future courses will consider the potential utility of this information, such as modifying course designs and outcome expectations.

117.146 146 The Good Life and How to Attain It: Lessons From the Experiences of People with High Functioning Autism Disorders. E. A. McNulty*¹, J. M. Montgomery² and M. Medved², (1)*Grant Macewan University*, (2)*University of Manitoba*

Background: People with high functioning autism spectrum disorders (ASD) usually have above average intelligence and many have talents

in narrow areas of knowledge or skill. However, their symptoms in the social and emotional realm frequently interfere with their efforts to achieve a satisfactory quality of life. Despite attempts to provide supports to increase positive outcomes, adults with ASD experience high rates of depression (Tsai, 2007) and poor quality of life (Jennes-Coussens et al., 2006). However, the voices of people with ASD are seldom heard in mainstream research, and successful coping strategies are largely unrecognized. This gap needs to be addressed.

Strength-based paradigms offer a unique way of approaching disability through a focus on strengths, rather than problems (Saleebey, 1992; Seligman, 2000). Important intervention information can be found by identifying successful adaptations and using the skills involved to produce better outcomes (see Seligman, 2000). Strength-based approaches emphasize empowerment, collaboration and "voice" (Brun & Rapp, 2001). These principles are central to this research project.

Objectives: The aim of this study was to determine, using a strengths-based/positive psychology lens, how people with high-functioning ASD defined "the good life", a concept popularized by Seligman (2000) and found to be instrumental in achieving positive life outcomes. Further, respondents were asked what they viewed as barriers or supports in achieving it, how they cope with the problems they encounter, and what they see as solutions to overcoming obstacles.

Methods: The primary method used in the research was in-depth interviews of 11 adults with high functioning ASD where the above stated objectives were explored. The interviews were recorded and transcribed verbatim. Interviews were analyzed to identify common themes and implications for improved support.

Results: The participants generally described "the good life" as attaining the goals that neurotypical individuals take for granted. For example, having meaningful adequately-paid work was a primary theme. Other goals included living independently, having satisfactory relationships, being able to spend time on their hobbies and interests, and being accepted as differently-abled rather than disabled. Participants reported that

lack of awareness and knowledge about autism results in policy and service barriers, which in turn lead to unrealistic expectations for people with high functioning ASD, and less than satisfactory outcomes.

Conclusions: There is a need for increased education and awareness about autism spectrum disorders in the wider community, especially in educational systems, in workplaces, and in agencies that help people with "disabilities". Improved understanding of autism is a necessary precursor to the development of policy and services that better reflect the needs of people with high functioning ASD. Better outcomes and an improved quality of life for people on the autism spectrum can only be achieved if the voices of people with ASD are heard with regard to their experiences and needs. Results of this study will be discussed in terms of the specific implications for individual supports and policies that participants identified.

117.147 147 Predictors of Parent-Child Interaction Style in Dyads Where Children Have Autism. K. Hudry*¹, C. R. Aldred², S. Wigham³, J. Green², K. Leadbitter², K. Temple³, K. Barlow³, H. McConachie³ and T. PACT Consortium², (1)*Olga Tennison Autism Research Centre*, (2)*University of Manchester*, (3)*Newcastle University*

Background: Promising results from some recent parent-mediated intervention trials suggest that that the communication skills of young children with autism can be improved via parental adoption of responsive/synchronous interaction styles. Only limited research has yet, however, considered potential determinants of habitual parent-child interaction style, prior to the delivery of any intervention,

Objectives: The current study undertook to comprehensively examine the associations among various individual-difference factors and concurrent measures of dyadic interaction style.

Methods: Within the large, well-characterized Preschool Autism Communication Trial cohort of dyads including children with core autism (see Green et al., 2010), baseline parent-child free-play interaction tapes have been rated using the novel Dyadic Communication Measure for Autism (DCMA). Coded for Parent Synchrony, Child Initiation, and Shared Attention are delineated and the current study examined associations

among these interaction measures, along with measures of family demographic characteristics, scores from standardized child assessments, and other examiner-rating scales.

Results: Various child factors (e.g., age, non-verbal and language ability levels, symptom presentation, etc.), but no parent or familial factors, presented significant association with the interaction measures. When entered as predictors, within individual regression analyses, child language age-equivalence carried unique significant predictive value for each of Parent Synchrony, Child Initiation and Shared Attention. Observed repetitive/stereotyped behaviour symptoms were also important predictors of Shared Attention. The three interaction measures were themselves moderately highly correlated, and carried substantive predictive value alongside child language ability and repetitive behaviour symptoms.

Conclusions: Variability in parent-child interaction styles, in the context of childhood autism, appears to be driven by concurrent language level of the child, more so than child age, specific social-communication symptom presentation, or non-verbal developmental/cognitive level. Beyond this factor, only repetitive behaviour symptoms appear to provide additional unique predictive value for one the particular aspect of dyadic shared attention, and numerous other parent and familial factors appear relatively unimportant. Aspects of the interaction style may also, however, act in important ways to maintain the adopted style of a given dyad.

117.148 148 The Effect of Semantic Context On Prosodic Processing Across the Autism Spectrum. A. M. Petrou*¹, M. E. Stewart¹, M. Ota², S. Peppe³ and J. McCann³, (1)*Heriot-Watt University*, (2)*University of Edinburgh*, (3)*Queen Margaret University*

Background: Children with autism spectrum conditions (ASC) display difficulties in interpreting contrastive stress (Paul et al., 2005; Peppé et al., 2007). This may be due to the reduced use of contextual information that is typically used to guide meaning (Happé & Frith, 2006).

Objectives: To assess the influence of semantic context on prosodic processing in ASC and

typically-developed adults with different degrees of autistic character traits.

Methods: The study was divided into two parts. Part one compared 19 young adults with High-Functioning Autism or Asperger's syndrome (HFA/AS) with 19 IQ-matched typically-developed young adults. Part two assessed the relationship between autistic traits in 68 typically-developed young adults. The individuals with HFA/AS were given the Autism Diagnostic Observation Schedule (ADOS; Lord et al., 1999). All participants completed the Raven's (Raven, Raven, & Court, 1998), the Millhill, the Autism-Spectrum Quotient (Baron-Cohen et al., 2001a), and two tests of prosodic processing. These measured the accuracy and response times of the listeners' ability to identify contrastive stress. In Test A, the placement of contrastive stress was contextually congruent for some items but incongruent for others. Test B measured discrimination of stress positions in laryngeal recordings with no discernible semantic or lexical information.

Results: Part One: The Raven's-matched HFA/AS sample showed a significant main effect of Congruency (accuracy, $F(1,36)=6.12$, $p<0.05$; RT, $F(1,36)=20.14$, $p<0.001$); performance in congruent trials was significantly better than in incongruent trials (accuracy, $t(37)=2.51$, $p<0.05$; RT, $t(37)=-4.56$, $p<0.001$). There was no significant main effect of Group or Group x Congruency interaction. However, there was a significant positive correlation between the Millhill and the Raven's with accuracy in the congruent trials in Test A ($r=0.53$, $r=0.50$; $p<0.05$, respectively) and between the Millhill and accuracy in Test B ($r=0.34$, $p<0.05$). Part Two: The typically-developed sample performed significantly better in congruent trials than in incongruent trials (accuracy, $t(67)=3.36$, $p<0.01$; RT, $t(67)=-4.05$, $p<0.001$). Performance was not related to autistic traits. However, there was a significant positive correlation between the Millhill and accuracy ($r=0.25$, $p<0.05$) and a significant negative correlation between the Millhill and RT ($r=-0.25$, $p<0.05$) in the congruent trials in Test A. There were no relationships between autistic traits and performance of prosodic processing in Test B.

Conclusions: The identification of contrastive stress is influenced by congruency with semantic

context, but this effect is not reduced as a function of increasing autistic traits in those with and without HFA/AS. Difficulties with contrastive stress were not found in the HFA/AS sample nor was performance related to autistic traits. The current sample was an adult one; there may be fewer difficulties with contrastive stress in this age group as prosodic skills develop gradually into adulthood (Wells, Peppé, & Goulandris, 2004). Further research is needed (a) to assess whether reduced processing of contrastive stress in semantic context is not captured by the current task or sample and (b) to understand the roles of verbal and nonverbal IQ on identification of contrastive stress.

117.149 149 'Think', 'Feel', 'React' - Exploring Anxiety in Autism Spectrum Disorder (ASD): The Role of Executive and Sensory Processing Dysfunctions. N. Darus*¹, J. Rodgers¹, D. Riby² and E. Janes³, (1)*School of Medical Sciences, Newcastle University*, (2)*Newcastle University*, (3)*School of Psychology, Newcastle University*

Background:

Autism Spectrum Disorders (ASD) are complex neurodevelopmental disorders with heterogeneity in terms of symptom profiles. Anxiety is a common comorbid condition affecting at least 40% of young people (Steensel et al., 2011). Anxiety contributes significantly to the challenges of living with an ASD for individuals and their families. The reasons for the elevated rates of anxiety associated with ASD are poorly understood. Executive Function difficulties (EF) and Sensory Processing (SP) atypicalities have both been associated with the presence of anxiety in ASD. However, the individual and shared contribution of these characteristics to anxiety in individuals with ASD is not fully understood.

Objectives:

The aim of this study is to investigate anxiety in children with ASD in relation to their EF and SP profiles. This will help to identify anxiety subtypes in relation to ASD specific phenotypes based on these characteristics.

Methods:

40 Young people with ASD aged between 8 and 16 years and their parents are being recruited. Self

and parent reports of anxiety, parent reports of sensory difficulties and neuropsychological assessment of executive function, form the basis of our protocol. Parents and young people will complete the Spence Anxiety Scales (SCAS), parents will complete the Short Sensory profile and the child will undertake a range of neuropsychological assessments based in the NEPSY battery. Cluster Analytic techniques will be used to enable subgroups based on executive, sensory and anxiety profiles to be identified.

Results:

This study is in the data collection stage, to date eleven families have been recruited. Data collection will be completed and findings will be available by May 2013.

Conclusions:

This research is a first step towards looking at the neuropsychological and sensory deficits which may underpin anxiety disorders in autism. The use of cluster analytic techniques will enable the heterogeneity of ASD to be taken into account and enable an understanding the relationships between and variations in the influence of these variables. It is hoped that this in turn will enable significant future advances in the development of individualized assessment and treatment approaches for young individual with ASD experiencing anxiety.

117.150 150 Language-Gestures Relationship in Narrative Production of Children with Autism Spectrum Disorders. S. Cuva*¹, P. Venuti¹, I. Dalvit¹, M. Mastrogiuseppe¹, P. Rigo¹ and O. Capirci², (1)*University of Trento*, (2)*National Research Council of Italy (CNR)*

Background:

Narratives provide an excellent measure of children's spontaneous language. Despite this, narrative ability of patients with Autism Spectrum Disorders (ASD) has not been widely investigated. To date is known that, compared with those of typically developing children, narratives of people with ASD are shorter and less complex and that their lack of social awareness affects the overall narrative quality and communicative strength (Tager-Flusberg et al., 1987). Of great importance is also the relationship between gestures and

language: in typical development, in fact, gestures are used to contribute to text coherence as well as to pragmatic content (Kendon 2004). This is of much interest since children with ASD usually do not use gestures to compensate for their communication difficulties, unlike children with other developmental disabilities and/or delays.

Objectives:

In this pilot study we analysed narrative production of children with ASD from the standpoint of the relationship between language and gestures.

Methods:

30 children were studied: 15 with high functioning ASD (mean chronological age (CA)=8,4 yrs Mean Mental Age (MA)=8,1 yrs) and 15 with typical development (Mean CA= 8,9 yrs Mean MA =8,5 yrs) matched for mental and chronological ages. Subjects were shown a 3 minute fragment from a Tom & Jerry cartoon and immediately after they were asked to tell the story they had just watched to one of their parents. Sessions were videotaped and video files were transcribed and coded using ELAN software (<http://www.mpi.nl/tools/>), as well as an annotation scheme (Capirci et al, 2011) including linguistic variables and information regarding narrative, pragmatics and gestures. A thorough assessment of children's functioning was used in order to make correlations between nonverbal communicative styles and other developmental variables.

Results:

From a linguistic point of view, the narratives of ASD children is composed of a number of clauses which makes it comparable with those of TD children. Despite this, children with ASD produce a significantly smaller number of gestures, compared with the TD group. Moreover, gesture use by children with ASD presents some formal and semantic peculiarity on the execution's strategies and on relations – both semantic and temporal – between the gestural and vocal elements of the utterance. The few gestures produced are not used to add value to the content of spoken language; instead they seem to be

produced *redundantly*, to underlie what the language would already be able to communicate.

Conclusions: The study of narratives, particularly from the standpoint of the relation between gestures and verbal production, might give many insights on the communicative capacity of children. This pilot study evidenced the paucity of gestural production and the atypical patterns of their use, both in terms of timing and of communicative meaning. Since the very specific impairment in communicative abilities and at the same time the wide heterogeneity within the ASD group, an important future area of research would be identifying different sub-groups of ASD in relation with gesture use both for theoretical and for therapeutic reasons; for example for identifying children that might eventually benefit from a gestural training.

117.151 151 Autism Mental Status Examination: A Preliminary Report of an Italian Version. V. Scandurra*¹, M. R. Scordo¹, C. Antonelli¹, R. Storino¹, C. Lorini² and R. Canitano³,
(1)Careggi University Hospital, (2)Florence University,
(3)University hospital of Siena

Background: The Autism Mental Status Examination (AMSE) is a new tool introduced to evaluate individuals with Autism Spectrum Disorders (ASDs). AMSE consists in a brief evaluation focused on the main features of Autism and combines clinical observations with information from parents. It is an eight items module to be administered in unstructured clinical setting. The use of this tool appears useful especially when Autism Diagnostic Observation Schedule (ADOS) and or Autism Diagnostic Interview-Revised (ADI-R) are not feasible.

Objectives: To develop an AMSE version applicable in Italy. To describe the application of AMSE to the Italian population of children and adolescents with suspect ASDs. To verify the reliability of AMSE Italian version.

Methods: 67 subjects, 9 F and 58 M, age 20 months – 18,2 ys range, mean ys 6,8 SD +/- 4,07, suspected to have an ASDs, have been evaluated in a clinical setting that included AMSE and ADOS evaluation.

Results: With a cut-off of 5, as proposed by the USA authors, we were able to correctly classified

91% of the sample. In the Italian experience AMSE allowed a correct classification of ASD according to ADOS criteria and clinical evaluation.

Conclusions: This is preliminary report of an ongoing study aimed at replicating and validating the findings obtained with the first study using AMSE. The main positive finding is regarding classification accuracy of ASD. AMSE holds promise as a standardized and rapid autism-focused mental status examination.

117.152 152 Psychometric Features of the Pictorial Infant

Communication Scales (PICS) in Preschool-Aged Children with ASD. C. S. Ghilain*¹, M. V. Parladé², M. McBee³, D. Coman¹, P. Durham¹, M. Alessandri¹, A. Gutierrez⁴, K. Hume⁵, B. Boyd⁶ and S. Odom³, (1)University of Miami, (2)University of Pittsburgh, (3)University of North Carolina, (4)Florida International University, (5)University of North Carolina, Chapel Hill, (6)University of North Carolina at Chapel Hill

Background: Joint attention, commonly referred to as the ability to coordinate social attention, is a crucial milestone in the development of communication (Bakeman & Adamson, 1984; Mundy et al., 2007). It is also a significant area of skill deficit in children with ASD (Diagnostic & Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV-TR) 2000; Kasari, Freeman, & Paparella, 2006). While reliable and valid parent-report measures of communication abilities are available (e.g., MacArthur-Bates Communicative Development Inventory; Fenson et al., 2002), assessment of joint attention has largely been limited to semi-structured, examiner-led interactions (e.g., Early Social Communication Scales; Mundy et al., 2003), which are time consuming and laborious to score. The Pictorial Infant Communication Scales (PICS; Delgado, Mundy, Venezia, & Block, 2003) was designed to address the need for an efficient parent-report measure of joint attention.

Objectives: To investigate the validity and underlying structure of the PICS for parent report of joint attention behavior in preschool-aged children with ASD.

Methods: The sample consisted of 197 preschool-aged children with ASD who were part of a completed multi-site study comparing comprehensive preschool programs for children with ASD. Children were between the ages of 3

and 5 years during enrollment, and were followed throughout the school year. Parents completed the PICS at the PRE-assessment time point.

The PICS is a brief, 16-item parent report questionnaire in which parents are asked to rate how frequently their child has displayed joint attention behaviors during the past two-week period using a 4-point Likert scale (i.e., 'not sure', 'never', 'sometimes' and 'frequently'). Each item is accompanied by pictures depicting the behaviors that parents are asked to rate. The PICS yields subscale scores for Initiates Joint Attention (IJA), Initiates Behavior Requests (IBR), and Responds to Joint Attention (RJA), as well as a Total Score. Correlations between the subscale scores were calculated, and internal consistency was examined for the total and subscale scores. The structure of the PICS was examined using confirmatory factor analyses (CFA).

Results: Construct validity was supported by intercorrelations among subscale scores. Specifically, the IBR and IJA scales were correlated at $r = 0.93$, while RJA and IJA were correlated at $r = 0.78$ and RJA and IBR were correlated at $r = 0.60$. The total score and subscales of the PICS were found to have a high degree of internal consistency (alpha coefficients ranging from 0.72 to 0.89). Results from the CFA provided support for the established three-factor model, broadly representing IJA, IBR, and RJA, $\chi^2(101) = 230.06$, $p < .0001$, CFI = 0.96, RMSEA = 0.082 (95% CI [0.07, 0.10], WRMR = 0.99). This model was preferred over a two-factor solution where IJA and IBR were collapsed, $\chi^2(2) = 22.91$, $p < .0001$.

Conclusions: Overall, the psychometric properties of the PICS appear promising, suggesting that it is a valid tool for measuring joint attention skills in preschool-aged children with ASD. Future research examining the concurrent and predictive relationships between the PICS and direct observation measures of joint attention and language would be beneficial.

117.154 154 Examining the Role of Cognitive Biases On Language Profiles in Autism Spectrum Disorders and Typical Development. S. B. Vanegas* and D. Davidson, Loyola University Chicago

Background: Evaluations of Weak Central Coherence (WCC) theory have suggested that

some children with Autism Spectrum Disorders (ASD) who demonstrate echolalia and hyperlexia may be processing linguistic components at the local or detail level, although comprehension may be limited (e.g., Newman, et al., 2007; Saldaña, Carreiras, & Frith, 2009; Schuler, 2003). Furthermore, Systemizing Theory proposes that children with ASD will exhibit difficulties in acquiring and producing functional language (Baron-Cohen, 2006). When learning language, children with autism will seek out lawful systems; however, considering the many exceptions within language structure and meaning, children with ASD experience difficulty establishing concrete rules to follow.

Objectives: It is well established that children with ASD may experience difficulties with language, however, many have only focused on identifying the specific areas of difficulties. To better inform language interventions, it is important to understand the underlying factors that influence specific language profiles. The inconsistency with English language structure, form, meaning, and usage creates a difficult medium for children with ASD to engage in communication, particularly if being driven by local features or set rules. The current study examined the role of cognitive biases on language development in ASD.

Methods: Children between 7 and 11 years of age with and without an ASD diagnosis (i.e., High-Functioning Autism, Asperger Syndrome) were included in the study. Two sets of measures were administered to assess cognitive biases. Weak Central Coherence measures included the Children's Embedded Figures Test (CEFT; Witkin, Oltman, Raskin, & Karp, 1971) and the Sentence Completion Task (SCT; Booth & Happé, 2010). These measures provided an assessment of visual and linguistic local processing. Systemizing measures included the Systemizing Quotient-Child Version (SQ-C; Auyeung et al., 2009) and the Picture Sequencing Test (PST; Baron-Cohen, Leslie & Frith, 1986). These measures provided an assessment of rule-based processing. To evaluate children's language profiles, the Core Language subtests of the Clinical Evaluation of Language Fundamentals - 4 (CELF-4; Semel, Wiig, & Secord, 2003) were administered. Parent-reported autism traits were evaluated using the Autism Spectrum Quotient - Child Version (ASQ). All tasks were administered in one session.

Results: Following the procedure used by Loth, Gomez, and Happé (2008), composite scores were created for local processing based on the CEFT and the SCT and for systemizing based on the SQ-C and the PST. Preliminary analyses suggest that there may be distinct underlying factors that influence language development in children with ASD. The Systemizing Composite was a significant predictor of core language abilities in children with HFA, $R^2 = .532$, $F(1, 7) = 7.968$, $p < .05$. However, parent-reported autism traits were the only significant predictor of core language abilities in children with AS, $R^2 = .768$, $F(1, 9) = 32.959$, $p < .001$. Further analyses will evaluate specific language components assessed within the core subtests of the CELF-4 (e.g., morphology, syntax, semantics).

Conclusions: The preliminary results suggest that children with HFA may be utilizing more systematic approaches in their linguistic abilities. Therefore it is important to include rule-based strategies in the intervention plans and curriculum for children with HFA.

117.155 155 Social Information Processing Skills in Relation to Emotion Recognition, Theory of Mind, and Pragmatic Language in Children with and without Autism Spectrum Disorders. N. M. Russo-Ponsaran*, C. McKown, J. K. Johnson, A. Allen and B. Evans-Smith, *Rush University Medical Center*

Background: Social impairment is a hallmark of children with autism spectrum disorder (ASDs). Children's social information processing (SIP) skills, or the ability to identify, process, and solve complex social problems, are associated with social success. Therefore it is not surprising that many children with ASDs are deficient in SIP skills. Yet it is unclear what other social-emotional skills, or deficits, contribute to their SIP challenges.

Objectives: The current study assessed the relationship between SIP skills and other social-emotional skills of emotion recognition, theory of mind, and pragmatic language in children with and without ASDs.

Methods: Forty-one children with ASDs (38 males) and 159 typically-developing (TD) peers between 5-14 years old, with $IQ \geq 85$, participated. Diagnoses were confirmed with the ADI-R and ADOS. For the SIP assessment, children were read

five hypothetical social problems, such as being bumped by a peer or having to compromise with a peer. After each description, a theoretically-based interview was conducted. Questions mirrored steps in the Crick and Dodge SIP model and included questions tapping into problem encoding, goal generation, and solution competency. Verbatim responses were coded by trained raters who achieved good reliability ($\alpha = .83$ to $.95$). Children also completed multiple choice tests of emotion recognition (faces, prosody, postures, and gait), a theory of mind test (Strange Stories), and a pragmatic judgment subtest from the Comprehensive Assessment of Spoken Language.

Results: Both groups showed relationships between problem encoding and pragmatic language, gait recognition, and theory of mind ($r \geq .3$, $p \leq .003$), as well as between solution competency and pragmatic language ($r \geq .398$, $p \leq .010$). Unique correlations within the ASD group showed that problem encoding was positively and significantly related to recognition of prosody ($r = .34$, $p = .028$) and posture ($r = .33$, $p = .034$); goal generation was uniquely related pragmatic language ($r = .428$, $p = .005$); and solution competency was correlated with gait ($r = .326$, $p = .037$). Unique to the TD group, problem encoding was positively associated with the facial affect ($r = .327$, $p < .001$). When correlations differed between groups, regression analysis was used to determine whether the relationships function the same or differently in each group. A significant interaction was found for goal generation and pragmatic language ($B = .537$, $F(3,196) = 14.979$, $p = .018$), indicating that higher scores on pragmatic language tasks had a larger influence on goal generation scores only within the ASD group.

Conclusions: These findings suggest that the antecedents of SIP in children with ASDs are, in some cases, like those in TD children. However, these findings also suggest that some antecedents of SIP in ASDs are qualitatively different than those in TD children. Further research is necessary to understand the manner in which pathways to successful SIP in ASDs resemble and differ from pathways to SIP in TD children. A more complete understanding of the developmental processes underlying SIP in ASDs has potential to inform assessment and treatment planning.

117.156 156 The Association of Emotion Dysregulation to Core Features of the Autism Spectrum Disorder. A. C. Samson^{*1}, J. J. Gross¹, S. Cormenzana², K. J. J. Parker³ and A. Y. Hardan³, (1)Stanford University, (2)Universidad de Deusto, (3)Stanford University School of Medicine

Background : Autism Spectrum Disorder (ASD) is a severe neurodevelopmental disorder characterized by impairments in social communication/interaction, restricted interest, and repetitive behavior. While emotion dysregulation is not typically considered a core deficit in ASD, there is an increased recognition of the frequency of the associated severe emotional disturbances. Evidence suggests that maladaptive emotional responses are common in ASD and there are hints that it might impair functioning. However, limited information is available on the potential relationship between emotion regulation difficulties and clinical deficits in ASD.

Objectives : The aim of the present study was to examine the relationship of emotion dysregulation in children and adolescents with ASD and several clinical features such as social/communication deficits, sensory abnormalities, cognitive functioning and adaptive abilities.

Methods : An emotion dysregulation index (EDI) was developed on the basis of expert ratings of the Child Behavior Checklist (CBCL) items. Eighteen items were determined to best represent emotion dysregulation and were included in the index. To examine the association between emotion dysregulation and clinical features of autism, the relationships between the EDI and the Social Responsiveness Scale (SRS), the Sensory Profile Questionnaire (SPQ), the Stanford Binet, and the Vineland Adaptive Behavior Scale were assessed in a sample of children and adolescents (6-18 years) with ASD, and typically developing (TD) controls. Data from 51 youth with ASD and 32 controls were included in the current analyses. ASD (41 males, 10 females) and TD participants (20 males, 12 females) did not differ in age ($F(1,82) = .03$, ns) and gender ($\chi^2(1) = 3.21$, ns). ASD diagnosis was established based on the administration of the Autism Diagnostic Interview-Revised, the Autism Observation Schedule, and expert clinical opinion.

Results : The computed EDI had good psychometric properties (Cronbach's alpha: $.89$).

The EDI did not correlate with age ($r=.05$, ns), and did not differ between males and females ($F(1,81)=3.36$, ns). As expected, differences were observed between ASD and TD on several scales including the EDI, IQ, and SRS. Within the ASD participants, the EDI correlated with SRS (e.g., *total score*: $r=.51$, $p<.01$), and several of the Vineland domains (e.g., coping skills, $r=-.48$, $p<.01$; sum of socialization, $r=-.39$, $p<.05$) and sensory factors (e.g., sensory seeking, $r=-.62$, $p<.001$; auditory processing, $r=-.50$, $p<.01$). No association was found between the EDI and cognitive functioning.

Conclusions : To our knowledge, this is the first study to bridge emotion dysregulation and deficits in core features as well as cognitive and adaptive functioning in children and adolescents with ASD. Our findings indicate that social deficits, coping skills, and sensory sensitivities may be related to emotion dysregulation. Emotion dysregulation might be related to certain core features of ASD warranting the development of effective therapeutic strategies targeting these emotional deficits to optimize long-term outcome.

117.158 158 The Relationship Between Social Anxiety and Loneliness Among Young Adults with Autism Spectrum Disorders. M. K. Fitzpatrick*¹, T. Bayrami¹, D. Janulaitis², S. Bates³, J. Hopkins⁴ and E. Laugeson⁵, (1)*The Help Group-UCLA Autism Research Alliance*, (2)*The Help Group - UCLA Autism Research Alliance*, (3)*UCLA PEERS Program*, (4)*UCLA PEERS Clinic*, (5)*UCLA Semel Institute for Neuroscience & Human Behavior*

Background:

Individuals with Autism Spectrum Disorders (ASD) often exhibit social deficits that may negatively impact their psychosocial functioning and interpersonal relationships. While the majority of research literature in this area has focused on school aged children on the spectrum, less research has examined correlates of social functioning among adults with ASD. Research suggests impaired social functioning in children with ASD may be associated with a higher incidence of social ridicule and peer rejection; in turn, possibly leading to greater feelings of loneliness and social isolation (Bauminger, 2003). Moreover, children with ASD are also at greater risk for experiencing social anxiety than typically developing youth (Bellini, 2004), which may also be related to greater self-perceived loneliness and

isolation. However, the relationship between social anxiety and loneliness among young adults with ASD has yet to be explored.

Objectives:

The present study aims to examine the relationship between self-perceived social anxiety and feelings of loneliness in young adults with ASD without intellectual disabilities.

Methods:

Participants included 17 young adults (14 males and 3 females) ranging from 18-27 years of age ($M = 21.3$, $SD = 2.78$) presenting for treatment through the UCLA PEERS[®] for Young Adults program, an evidence-based social skills group for individuals with ASD. In order to examine the relationship between social anxiety and subjective loneliness, participants completed the Social Anxiety Scale (SAS; La Greca, 1999) and the Social and Emotional Loneliness Scale for Adults (SELSA; DiTomasso & Spinner, 1993) prior to treatment. Pearson correlations were calculated to examine the relationship between total and subscale scores of the SAS and SELSA.

Results:

Preliminary results reveal that elevation on the SAS total score, which assesses overall degree of self-perceived social anxiety, is correlated with higher scores on the SELSA Social Relationships subscale ($p<.04$), which measures the degree of self-reported loneliness in friendships. Additionally, higher scores on the SAS Fear of Negative Evaluation subscale, which assesses the level of concern regarding peer's negative appraisal, is correlated with elevations on the SELSA total score ($p<.03$), which measures overall self-perceived loneliness in relation to family, romantic relationships, and friendships. The SAS Fear of Negative Evaluation subscale is also correlated with the SELSA Social Relationships subscale ($p<.001$). No other statistically significant correlations were observed between the SAS and SELSA.

Conclusions:

Preliminary results suggest that young adults experiencing greater social anxiety are also subject to greater loneliness in relation to their friendships. Furthermore, young adults who endorse greater fear of negative evaluations from their peers are more likely to experience greater overall loneliness in relation to family, romantic relationships, and friendships. This research represents the first study to investigate the relationship between social anxiety and self-perceived loneliness in young adults with ASD without intellectual disabilities, and suggests the need for more targeted interventions to decrease social anxiety in this population.

117.159 159 Mother–Child Dyadic Interaction in Preschoolers with ASD: Emotion Regulation and Cortisol Levels During Positive and Negative Emotion Eliciting Situations. S. Ostfeld Etzion*, O. Golan, Y. Hirschler Guttenberg and R. Feldman, *Bar-Ilan University*

Background:

Clinical experience and research findings indicate that emotional difficulties are more common among children with Autism Spectrum Disorders (ASD), as compared to typically developing (TD) children. The ability to regulate emotions is a global developmental achievement at the preschool years and difficulties in emotion regulation (ER) at this stage have been associated with less optimal development across childhood and adolescence. Developmental research suggests that children use a variety of emotion regulation strategies (such as diversion, self-soothing) to help regulate negative and positive emotional states, such as fear, anger, or joy, with varying degrees of efficacy. The development of ER strategies depends on physiological control systems (e.g. sensory sensitivity, physiological arousal), but also on practice in the context of parent-child interaction.

Objectives:

To compare the ER strategies of children with ASD to those of TD children during presentation of positive and negative emotions and during mother-child interaction. The effect of children's stress reactivity, as measured by Cortisol levels, on ER strategies was also explored.

Methods:

The study included 77 parents and preschoolers-38 pre-school children with ASD and 39 TD controls, matched for gender and mental age. Children were videotaped during mother-child free-play, and two procedures eliciting mild frustration: toy-removal and parental still-face paradigms. Videos were micro-coded for regulatory behaviors and the quality of the interaction was globally coded using the Coding of Interactive Behavior protocol. Cortisol levels from mother and child were measured at baseline and following the stressors.

Results:

Children with ASD exhibited less mature ER strategies as compared to TD children in the regulation of both negative and positive emotions. Similarly, cortisol reactivity patterns were less optimal in children with ASD and were correlated with ER patterns. During the still-face paradigm children with ASD used simpler ER strategies, such as protest, withdrawal, or idiosyncratic behavior, and were less efficient in employing more complex strategies, such as distraction, or use of play to manage negative emotions. There were no differences in ER strategies on the toy-removal paradigm, in which parents were able to be active soothers. During parent-child interaction, although children with ASD showed less social engagement and compliance than TD children, no differences were found in parental sensitivity, intrusiveness, and limit-setting behavior.

Conclusions:

The study is among the first to demonstrate ER difficulties in preschoolers with ASD during the regulation of emotions within a social context. Despite deficient ER in children with ASD, their mothers show similar parenting behaviors to mothers of TD children. The study illustrates the importance of parental support in scaffoldings ER strategies for children with ASD. These findings have important clinical implications for parents of young children with ASD.

117.160 160 Sexual Knowledge, Self-Efficacy, and Risky Behaviours: Are Young Adults with ASD At Risk?. S. M. Brown*, M. A. Vecili and J. A. Weiss, *York University*

Background: Knowledge and self-perceptions are important factors in the development of safe sexual practices and healthy relationships for typical developing individuals (Ajzen, 1991; Bandura, 1986; Bandura, 2001; Fisher & Fisher, 1992; Berten & Van Rossem, 2009). Parents and peers have been found to be particularly important sources of such knowledge (Beal, Ausiello, & Perrin, 2001; Dilorio, Kelly, & Hockenberry-Eaton, 1999; Whitaker & Miller, 2000). Given the specific areas of deficits found in people with Autism Spectrum Disorders (ASD; particularly social relationships and social-cognitive processing), many may miss or misunderstand important sexual knowledge gaining opportunities. In addition, many parents of individuals with ASD may lack self-efficacy in explaining sexuality and sexual-related topics (Meister, Honeyman, Norlack, Peirce, 1994; Konstantareas & Lunsy, 1997). Although individuals with ASD have been found to display an interest in sexual interactions and engage in sexual behaviours (Van Bourgondien, Reichle, & Palmer, 1997; Ousley & Mesibov, 1991), they may not have appropriate knowledge or confidence in their abilities, and consequently may be at risk for participating in risky sexual exchanges.

Objectives: The purpose of the current study is to explore sexual knowledge (actual knowledge, perceived knowledge, and sources of information) and self-perceptions of competence in high functioning individuals with ASD as they compare to their typical developing counterparts. The current study will also examine how these factors relate to risky sexual behaviours in both groups.

Methods: Fifty individuals with high functioning ASD were matched by chronological age to 50 typical developing individuals. All participants were between 18 to 30 years of age, lived in North America, and were willing to participate in an online survey. Participants completed the Autism Spectrum Quotient (AQ-adult; Baron-Cohen, Wheelwright, Skinner, Martin & Clubley, 2001), Sexualized Behavior Scale (Mehzabin & Stokes, 2011), Revised Knowledge of Sexual Health (Walsh & Ward, 2010), and researcher created questionnaires regarding sexual knowledge sources, perceived knowledge, sexual demographics, and sexual experiences and behaviors.

Results: The survey has been piloted with typical developing participants and data collection is ongoing. The interaction between actual knowledge and self-perception of knowledge will be examined as it relates to risky sexual behaviours. The relationship between actual knowledge and where the participants obtained their knowledge (knowledge sources) will be examined.

Conclusions: The results of this study will provide an understanding of sexual health knowledge in the adult ASD population and how this relates to risky sexual behavior. It will provide important implications for educational interventions focusing on sexual knowledge.

117.161 161 Social Motivation As a Predictor of Decreased Problem Behaviors in Adolescents with ASD Following the UCLA PEERS® Program. Y. Bolourian*¹, J. Hopkins¹, S. Bates² and E. Laugeson³, (1)UCLA PEERS Clinic, (2)UCLA PEERS Program, (3)UCLA Semel Institute for Neuroscience & Human Behavior

Background:

Adolescents with Autism Spectrum Disorders (ASD) show an array of poor social skills, as well as problem behaviors associated with their disability. Problem behaviors may include aggression, hyperactivity, depression, anxiety, and perseveration (Gresham & Elliot, 2008). These problem behaviors are often associated with difficulties initiating and maintaining social interactions and meaningful relationships, and may also interfere with the acquisition of social skills during treatment (Gresham, Elliot, & Kettler, 2010). Despite treatment obstacles, studies have shown that many adolescents with ASD are eager to increase and enrich their peer interactions and relationships. Thus, identifying the factors that predict treatment outcome related to decreased problem behaviors may be useful in distinguishing those who are likely to benefit from targeted social skills treatment.

Objectives:

The present study examines the extent to which social motivation predicts decreased problem behaviors following the implementation of a parent-assisted social skills intervention for adolescents with ASD.

Methods:

Seventy-four adolescents with ASD, ranging from 11-18 years of age ($M = 14.04$; $SD = 1.80$), and their parents participated in the Program for the Education and Enrichment of Relational Skills (PEERS®), a manualized, evidence-based, parent-assisted social skills intervention for youth with ASD. Participants attended weekly 90-minute group treatment sessions over a 14-week period. Targeted skills included but were not limited to: conversational skills; peer entry and exiting skills; appropriate use of humor; good host behavior during get-togethers; good sportsmanship; strategies for handling rejection including teasing, bullying, arguments, and rumors/gossip; and strategies for changing bad reputations. Skills were taught through didactic instruction using concrete rules and steps of social etiquette in conjunction with role-playing exercises, in-group activities, and parent-assisted weekly socialization homework assignments outside of the group.

In order to understand the relationship between social motivation and decreased problem behaviors, parents completed the Social Responsiveness Scale-Parent Report (SRS-P; Constantino, 2005) at baseline, which assesses social motivation among adolescents with ASD, and the Social Skills Improvement System-Parent Form (SSIS-P; Gresham & Elliot, 2008) at pre- and post-test to assess changes in problem behaviors following treatment. Pearson correlations were calculated to examine the relationship between the SRS-P Social Motivation Subscale and the SSIS-P Problem Behavior subscales.

Results:

Results reveal that higher parent-reported baseline scores on the SRS Social Motivation Subscale predict decreased problem behaviors on the SSIS-P Hyperactivity/Inattention ($p < .05$) and Autism Spectrum ($p < .03$) Subscales following treatment. Social Motivation on the SRS-P was not significantly correlated with other SSIS-P Problem Behavior subscales

Conclusions:

These findings suggest that adolescents with ASD who demonstrate greater social motivation and drive to interact with peers prior to treatment are less likely to display problem behaviors such as hyperactivity, impulsivity, inattention, and autism spectrum symptoms following PEERS®, an evidence-based, parent-assisted social skills program.

117.162 162 Methods for Assessing Language in School-Age Children with Autism and Intellectual Disability. A. Sterling*, E. Haebig and S. Schroeder, *University of Wisconsin-Madison*

Background: The language phenotype of autism is characterized by delays in expressive language vocabulary, pragmatics, and grammar. This phenotype is closely tied to general language comprehension, and has been compared to other disorders like Specific Language Impairment and disorders with similar behavioral phenotypes (e.g., fragile X). Little has been done on the best method for assessing language in children with autism with an intellectual disability. Research in fragile X has found children perform at nonverbal mental age expectations on standardized tests, but below expectations on a language sample. Language samples require social engagement, and can be particularly challenging for individuals with poor pragmatic skills or those with high levels of social anxiety, both found in autism.

Objectives: To examine the best assessment method for language in children with autism who also have an intellectual disability using a variety of methods commonly used in both the research and clinical domains. We included a comparison group of nonverbal mental age matched children with fragile X syndrome.

Methods: Seven boys with autism have completed the study (study is ongoing, anticipated number of participants 26), as well as 14 boys with fragile X syndrome between the ages of 9-16 years. Assessments included standardized language assessments: receptive and expressive vocabulary (PPVT and EVT), receptive and expressive grammar (i.e., TEGI, CELF), as well as a nonverbal IQ test (Leiter brief IQ), a language sample, and a sentence imitation task. Additionally each participant completed the Autism Diagnostic Observation Schedule (ADOS) and parents completed the Autism Diagnostic Interview-Revised (ADI-R). The Childhood Autism

Rating Scale was completed post-assessment. The language samples, sentence imitation task, and ADOS were transcribed using standard language transcription procedures, and analyzed using the Systematic Analysis of Language Transcripts (SALT; Miller & Chapman, 2000). Transcripts were analyzed for standard language measures including number of utterances, number of words, grammatical complexity (MLU), and measures of dysfluencies (e.g., repetitive speech, incomplete sentences).

Results: Preliminary results indicate the boys with autism show a relative strength on the sentence imitation task (100% accuracy) and standardized assessments, but lower language levels on the conversation sample (mean MLU: 4.47). The boys with FXS demonstrated more impairment on the sentence imitation task (75% accuracy) and in the language sample (FXS MLU: 2.62).

Conclusions: The boys with autism demonstrated a relative strength on both the sentence imitation task as well as the standardized tests. The language samples yielded less complex language compared to what would be expected based on standardized test performance, but more complexity compared to FXS. We will compare the language used in the language samples to the ADOS in order to look at contextual differences. The boys with FXS struggled with the sentence imitation task, but like autism, demonstrated a relative strength on the standardized assessment. While language samples are an important part of both clinical practice and research, preliminary evidence suggests they are not as informative in terms of the true picture of strengths and weaknesses for some aspects of language, in this case grammar.

117.163 163 Identifying Sub-Types of Responders to Intervention in Young Children with Autistic Spectrum Disorder. R. L. Young*¹, N. Brewer¹, M. T. Angley¹, L. Giles² and T. Windsor¹, (1)*Flinders University of South Australia*, (2)*Adelaide University*

Background:

The term Autism Spectrum Disorder (ASD) has been introduced to reflect the heterogeneity in presentation of disorders previously assigned to discrete diagnostic terms (e.g., Autistic Disorder, Asperger's Syndrome, Pervasive Developmental Disorder - Not Otherwise Specified; Diagnostic

and Statistical Manual of Mental Disorders, DSM-IV, DSM-5). Despite our understanding of the diversity in presentation of ASD, response to intervention has typically been evaluated in terms of overall improvement in treatment groups. It seems likely, however, that just as presentation differs between individuals, so too does response to intervention. Consistent with this perspective is the finding that a significant proportion of children who undertake early intervention do not make noticeable skill improvement (Bent & Hendren, 2010; Seltzer, Krauss, Shattuck, Orsmond et al., 2003; Goin-Koechel et al., 2007; Smith, 1999); in contrast, individuals who have received no intervention sometimes show gains consistent with those seen in treatment groups (Howlin, Magiati, & Charman, 2009). Our study aimed to identify clinically relevant behaviours and possibly phenotypes that might be indicative of better outcomes to treatment.

Objectives:

Our aim was to identify early behaviours that may be pivotal in determining response to treatment. These behaviours consisted of (a) "negative" symptomatology; the absence of which might undermine "typical" development (e.g., lack of shared enjoyment, social reciprocity, imitation and play) and (b) "positive" symptomatology (e.g., sensory sensitivity, stereotypical behaviours, jargon, gaze avoidance), the presence of which might do likewise.

Methods:

We examined this issue in the context of an on-campus, early behavioural intervention research program for infants with an ASD. In this study we used pre- and post-intervention behavioural measures to identify characteristics of children who varied in their response to an early intervention program. Data from 189 children were available for the analyses at the first three data points (0 weeks, 2 weeks, 18 weeks). Children were exposed to an applied behavior analysis (ABA) intervention program, with behavioural measures obtained pre-intervention, two weeks into intervention and 18 weeks after completion of clinic-based intervention. Children were then followed up after 2 years of independent intervention.

Results:

It was clear that for some children the response to intervention was far more positive than for others. Initial presentation was a meaningful indicator of the likelihood of response to intervention as indexed by measures of adaptive functioning (e.g., Childhood Rating Scale, Vineland Adaptive Behaviour Scale). Overall, these results suggest that early behavioural presentation can be used as a predictor of response to early intervention among children with autism. The behaviours pivotal to outcome and the possible interaction between positive and negative symptomatology are discussed.

Conclusions:

It is apparent that the absence of some behaviours undermines successful intervention using ABA techniques. Further, other symptomatology may interfere with typical development and reduce the likelihood of success. Intervention programs should focus on the specifics of these behaviours rather than the traditional focus on group outcomes. Successful sub-typing of individuals in terms of likely response to intervention has the potential to enable caregivers to make informed decisions about suitability of an intervention program.

117.164 164 Auditory Processing Skills and Joint Attention Abilities in Children with ASDs. R. Fadda¹, G. S. Doneddu², S. Congiu², G. Saba² and L. Ferretti², (1)University of Cagliari, (2)Azienda Ospedaliera Brotzu

Background: A number of studies demonstrated that almost 30% of children with Autism Spectrum Disorders (ASDs) are affected by Auditory Processing Disorders (Baranek, Foster & Berkson, 1997), which reduce their ability to attend, understand and remember information from verbal language. Although a number of recent studies highlighted the importance of auditory processing skills for language development in children with ASDs (Dawson & Wathing, 2000; Tager-Flusberg & Joseph, 2003; Khul, Coffey-Corina, Padden, Dawson, 2005), the relationship between Auditory Process Disorders and Joint Attention abilities, who are known to be an important precursor to language acquisition, has been rarely explored in children with ASDs.

Objectives: This study evaluates Joint Attention (JA) abilities in children with ASDs, measured by the means of an Eye Tracking paradigm, in relation to their auditory processing skills.

Methods: 35 children with ASDs (6 females), 31 with a diagnosis of Autism and 4 of PDD-NOS, aged between 46-137 months (mean age=88.37 months; SD=26), mean non-verbal level measured with the Leiter-R=77.03 (SD=18.43), participated in the study. 37 typically developing children (18 females), ranging in age from 39 to 79 months (mean age=51.76 months, SD=4.42) were included as controls. Auditory processing abilities were evaluated with a list of non-words (Cornoldi, Miato, Molin e Poli, 2009) and children with ASDs were divided into two groups, using the mean of the group of ASDs children as cut-off: a group with lower auditory processing skills (below the mean) and a group with average auditory processing skills (equal or above the mean). To evaluate JA abilities, the children were shown a video of a brief social interaction between two characters, by the means of a Tobii T60 Eye Tracker. The number of JA visual pattern (character A - object - character B) produced by participants when they visually explored the social scene were counted.

Results: 58% of the children with ASDs showed average auditory processing (mean number of correct non-words=51; sd=4.811) while 42% of them scored lower in auditory processing skills (mean number of correct non-words=37; ds=5.02). A between group ANOVA showed that the children with lower auditory processing skills produced a significantly lower number of JA visual patterns compared to the children with ASDs with average auditory processing abilities and to the TD controls ($F=8.094$; $df=2;71$; $p=0.01$). The two subgroups of children with ASDs did not differ for verbal and non-verbal abilities, as measured respectively by the Peabody Picture Vocabulary Test and by the Leiter-R.

Conclusions: These results seem to support the hypothesis of a relationship between social and linguistic processing in children with ASDs. Moreover, they highlight the importance of assessing auditory processing skills in these children, since difficulties in perceiving and segmenting linguistic information, together with a

lack of JA abilities can result in a significant disadvantage in language learning.

117.165 165 Infants' Repetitive Behaviour, Locomotor Development and Social-Communication Abilities. R. Fyfield*¹, S. R. Leekam² and D. F. Hay¹, (1)*Cardiff University*, (2)*School of Psychology, Cardiff University*

Background: By definition repetitive behaviours are considered to be symptoms of ASD, and are highlighted as potential indicators for ASD in current clinical practice. They represent one third of Wing and Gould's (1979) triad of impairments and are an essential part of diagnosis. Repetitive behaviours are commonly seen amongst typically developing infants; however, little information exists concerning normal variation amongst repetitive behaviours in community samples. It is imperative to understand repetitive behaviours from a broader developmental context in order to establish normative trends and frequencies.

Objectives: The present study of a nationally representative community sample addresses three main questions: (1) Are older infants less likely to use repetitive behaviours? (2) Are infants with more advanced motor development less likely to use repetitive behaviours? (3) Are repetitive behaviours negatively or positively associated with infants' social and communicative skills?

Methods: Repetitive behaviours were recorded in a sample of 243 11- to 14 month-old infants. Observational methods were used to record instances of two categories of repetitive behaviours (motor stereotypies and repetitive manipulation of objects) during free play and infants' turn-taking abilities with an examiner. Parents reported on the infants' motor development.

Results: Repetitive motor actions were negatively and significantly associated with age in months, locomotor ability and turn-taking abilities. Repetitive object manipulation was not associated with age, maturation or social skill.

Conclusions: The present findings allow us to begin to place repetitive behaviour within a normative development context which will inform studies of high-risk infants. The present cross-sectional findings suggest there might be a normative decline in motor stereotypies between

11 and 14 months but no similar decline in repetitive manipulations on objects, which remain common in typically developing one-year-olds. These cross-sectional data need to be confirmed in longitudinal analyses. However, the higher rates of motor stereotypies shown by infants with less mature locomotor and social skills suggests the continued use of repetitive motor actions in the second year of life might possibly be a sign of developmental delay and problems in social interaction relevant to ASD. In contrast, in this sample, repetitive operations on objects were age-normative, and not associated with motor immaturity or lack of social skill. Thus repetitive exploration of objects is not likely to be informative for attempts to identify early signs of ASD in this age range. Future attempts to diagnose ASD in the toddler years should distinguish between the two categories of repetitive behaviour.

117.166 166 Quantifying Social-Communicative Function in ASD Via a Structured Social Attribution Task. R. Burger-Caplan*¹, W. Jones² and A. Klin², (1)*Emory University*, (2)*Marcus Autism Center, Children's Healthcare of Atlanta & Emory University School of Medicine*

Background: With the move to an all-encompassing diagnostic classification – Autism Spectrum Disorders – from previously unsuccessful subtyping attempts, there will be renewed need for quantification measurements of the disability that have clinical and prescriptive validity. Individuals with ASD exhibit great difficulty in social cognitive tasks that require intuitive understanding of ambiguous social stimuli, these being less mediated by language, rote knowledge or explicit rules. Capitalizing on a classic social animation created by Heider & Simmel (1944), we previously quantified spontaneous narratives given after viewing the cartoon - in which geometric shapes enact a social story - and demonstrated significant social attribution deficits in higher functioning adolescents with ASD relative to matched controls (Klin, 2000), deficits that were not apparent in more traditional tests of social and mental state attribution. However, this procedure – the Social Attribution Task – required laborious codification of open-ended narratives and was impractical for more expansive usage. In this study, we tested the clinical utility of a simplified procedure in which 19 scenes from the original cartoon were

isolated and participants provided answers in a multiple-choice format.

Objectives: To examine the diagnostic discriminative utility of the Social Attribution Task – Multiple Choice (SAT-MC), and to assess its differential predictive power relative to social-communicative adaptive function, independent of verbal skill levels.

Methods: The SAT-MC was administered to a heterogeneous group of children with ASD characterized with standardized diagnostic procedures (N=23; Age range 4.5 to 12 years; VIQ range 62 to 146), and to a control group matched on chronological age and Verbal IQ (N=57). Adaptive skills in the areas of Communication, Socialization and Daily Living Skills were assessed with the Vineland Adaptive Behavior Scales. Correct answers on 19 items yielded a global SAT-MC score. Between-group comparisons on the SAT-MC score were performed to assess diagnostic discriminative utility. For the ASD group, correlational analyses between SAT-MC score and Vineland scores in the Communication and Social domains were performed to assess differential predictive utility, relative to the unrelated construct of Daily Living Skills. We performed correlations with Age and Verbal IQ in order to ensure that the SAT-MC taps on a developmental skill and is relatively independent from verbal skill level, respectively. Finally, individual SAT-MC items were analyzed for their specific discriminative power.

Results: Performance on the SAT-MC differed significantly between the ASD and TD groups. SAT-MC scores were positively correlated with age ($r = .474$) and were independent from Verbal IQ ($r = .236$). SAT-MC scores were strongly correlated with Vineland Communication ($r = .464$) and Socialization ($r = .482$) standard scores but not with Vineland Daily Living scores ($r = .116$). Item analyses revealed variability of individual items' diagnostic discriminative power.

Conclusions: The SAT-MC was shown to discriminate a heterogeneous group of children with ASD from matched controls, and to differentially predict levels of social and communicative adaptive skills independently from verbal function. This initial study corroborates previously demonstrated deficits in social

attribution and holds promise for quantification of skills that are essential for successful adaptation in real life.

117.167 167 Diminished Social Responses During Neurobehavioral Exam in Newborns At-Risk for Autism. S. J. Sheinkopf^{*1}, L. Andreozzi², E. J. Tenenbaum², A. L. Salisbury¹ and B. M. Lester², (1)*The Warren Alpert Medical School of Brown University*, (2)*Women & Infants Hospital*

Background: Diminished social responses and initiations have been observed late in the first year of life in infants at risk for autism. Findings of altered social responses earlier in infancy have been less consistent. Observational methods that include specific presses for responses to social (animate) and nonsocial (inanimate) stimuli may be sensitive to such differences in social responsiveness in early infancy.

Objectives: To investigate differences in responses to animate and inanimate stimuli in the newborn period for infants at risk for autism. A secondary goal was to explore other behavioral differences on neurobehavioral exam in at risk infants.

Methods: Nine (9) newborns were recruited from a study of infant siblings with autism (Autism Risk group; AR). Sibling diagnoses were confirmed for 6 of the children by best estimate clinical diagnosis plus above-threshold scores on the ADOS. These 6 AR infants were compared to a group of 45 newborns with no family history of autism recruited from an ongoing longitudinal study (Low Risk group; LR). All babies were administered the NICU Network Neurobehavioral Scales (NNNS; Lester & Tronick, 2004) at 2 to 4 weeks of age. The NNNS includes 6 procedures that press the baby to attend to, orient toward or visually track animate (examiner's voice and/or face) and inanimate (rattle/ball) stimuli (Animate auditory, visual and auditory+visual stimuli; Inanimate auditory, visual and auditory+visual stimuli). The NNNS examiner was naïve to risk group status. Statistical analyses utilized one-tailed T-tests of means on the a priori hypothesis that the AR group would show diminished responses to the animate stimuli. Summary scales overall are also available from the NNNS and have been explored on a post hoc basis.

Results: The Animate visual and auditory items were averaged, as were the Inanimate items. This

resulted in summary variables for Inanimate and Animate responses. The AR newborns showed diminished responses as compared to LR infants to the Animate items (AR 3.3 vs LR 5.2; $p=0.003$; $d= -1.3$). The AR and LR infants did not differ on the Inanimate summary measure (AR 5.0 vs LR 5.2, $p= 0.79$; $d= -0.2$). The difference in Animate responses was driven by statistically significant differences on Animate Visual ($p = 0.002$) and the Animate Auditory+Visual items ($p= 0.005$). There was a trend for diminished responses to Animate Auditory stimuli in the AR group ($p= 0.057$). Additional analyses have explored differences between the AR and LR groups on non-specific measures of stress response and broad neurobehavioral status on the NNNS.

Conclusions: This preliminary study suggests that infants at risk for autism show a diminished response to animate but not to inanimate stimuli in the newborn period. Other research has examined social responses in early to middle infancy in at risk babies, but results have been inconsistent and often subtle. While these findings require replication, they suggest that the nature of observational methods (i.e., the design of the behavioral assay) will affect the sensitivity to detect differences associated with risk for autism in very early infancy.

117.168 168 Orthography Facilitates Vocabulary Learning for (Some) Children with Autism Spectrum Disorders (ASD). R. Lucas*¹ and C. Norbury², (1)*Royal Holloway University of London*, (2)*Royal Holloway, University of London*

Background: Research has demonstrated that exposure to orthography facilitates oral vocabulary learning for typically developing (TD) children (Ricketts et al, 2009, 2011; Rosenthal & Ehri, 2008). To date there is no evidence that children with Autism Spectrum Disorders (ASD) use print to support learning but children with ASD are often exposed to pictures accompanied by words to support their communication.

Objectives: This study investigated whether children with ASD can use orthography to facilitate oral vocabulary learning and explicitly explored the influence of language and reading ability. It was hypothesised that children with ASD and age-appropriate structural language skills (ALN) would learn new vocabulary as efficiently as their TD peers, effectively using

orthography to assist their learning. Contrastingly the ASD language impaired children (ALI) would experience less benefit from orthography due to their poorer reading skills and the proportion of fixations on the orthography (as opposed to the picture) would be smaller than their TD and ALN peers.

Methods: Participants were 55 children age 8-12 years; 30 who had a formal diagnosis of ASD (ALN $n=15$, ALI $n=15$) and 25 TD peers. Participants were taught 16 low frequency concrete science words, for example 'breccia'. For half of the stimuli, the written word was presented alongside a picture of the target item (orthography present, OP); the remaining items were taught with orthography absent (OA). Eye-tracking attained fixation information during the learning phrase. Learning was assessed via three post-tests: picture naming, spoken word to picture matching and two-alternative-forced-choice spoken word to written word matching. Accuracy and response time (RT, for correct responses only) were recorded.

Results: The eye-tracking data indicated that during presentation of OP stimuli in the learning phrase, all three groups fixated on the picture more than the word. However, the ALI group had a larger proportion of fixations on the written word than the TD or ALN groups. With regards to the post-tests, picture naming accuracy was significantly greater for OP than OA stimuli and greater on day 2 than day 1 for all three groups. For the spoken word to picture and spoken word to written word matching tasks there was a main effect of orthography and of group. The facilitation of orthography was significant for the TD and ALN groups but not for their ALI peers, who were less accurate and had slower RT than the TD and ALN participants.

Conclusions: These results indicate that orthography facilitates vocabulary learning for ALN children, as it does for their TD peers. This suggests that the teaching of new oral vocabulary would benefit from the written form of the word being provided. ALI children did not benefit as extensively from the presence of orthography. However, the proportion of fixations on the written form was greater than expected, potentially indicating that despite their reading

difficulties the ALI children were attempting to utilise the written form to augment their learning.

117.169 169 Do Children with Autism Understand Communicative Intentions in a Hiding-Finding Game?. R. P. Hobson*¹, J. A. Hobson¹ and P. Rios², (1)*Institute of Child Health, UCL*, (2)*Harper House Children's Service*

Background: Most autism research on understanding communicative intentions has focussed on verbal communication (e.g., Eales, 1993; Happé, 1993). We have reported provisional evidence that children with autism often fail to grasp a person's head nods as intending to indicate location (Hobson, Garcia-Perez, & Lee, 2010). Here we modified a hiding-finding game inspired by Tomasello, Call and Gluckman (1997), who reported that children under 3 years, but not great apes, understood someone's conventional and unconventional actions as intending to inform about a hidden object's location.

Objectives: Our aim was to assess whether participants with autism would read one person's unconventionally expressed communicative intentions to help someone else. Participants were shown videotaped scenes involving a 'hider', 'finder' and 'helper' (played by trained child actors), and were asked to describe what happened in the vignette. The vignettes included different conditions which might have facilitated or hindered participants' understanding, such as whether the 'finder' was successful.

Methods: Participants were 15 children and adolescents with autism (5 girls, 10 boys: diagnosis confirmed with ADOS: Lord, Rutter & Goode, 1998) and a comparison group of 15 children without autism (5 girls, 10 boys) either typically developing ($n = 4$) or with learning/developmental disabilities ($n = 11$), matched for chronological age (Autism $M = 11$ years; 5 months and Comparison $M = 11$ years; 10 months) and the Expressive and Receptive Vocabulary subscales of the Test of Word Knowledge.

Participants viewed 11 videotaped scenarios of a hide-and-seek game. In nine of the clips, a 'helper' used an unconventional means to communicate to the 'seeker' where a hidden object was located e.g., by 'pointing' with a leg, or throwing an object in the direction of the hidden

object. Two final videotapes showed conventional pointing-to-inform. Following each clip, the tester asked the child to describe what happened, and then asked what each character said and did. Transcripts and the video-recording of participant responses were coded by judges unaware of diagnosis, for levels of (1) Understanding the Vignette, Kappa = .93; (2) Describing the Actions of the Helper, Kappa = .96; (3) Attributing Communicative Intent to the Helper, Kappa = .97, and (4) Need for Prompt to describe the sequence, Kappa = .97.

Results: Children with as well as without autism were able to interpret conventional points. On the other hand, participants with autism found it difficult to discern the communicative intent when someone tried to indicate a location using unconventional gestures or actions. Participants in the comparison group judged approximately two thirds ($M = 5.27$) of these vignettes in terms of the helper's intention to communicate something to the seeker, whereas the participants with autism made this judgement for fewer than one-third of the video vignettes ($M = 2.67$), $t(28) = 2.03$, $p < .05$. We shall provide further details on analysis as well as qualitative examples of responses.

Conclusions: Children with autism face difficulties in reading communicative intent to inform someone else, expressed in unconventional non-verbal communication, even when they can understand conventional pointing-to-inform.

117.170 170 Social Attention in 12- and 18-Month-Old Infants Later Diagnosed with Autism. A. R. Neal-Beevers*¹, S. J. Sheinkopf², T. P. Levine³, A. L. Johnson², B. M. Lester², L. L. LaGasse³, C. R. Bauer⁴, S. Shankaran⁵, H. Bada⁶, J. A. Hammond⁷, T. M. Whitaker⁸ and R. Higgins⁹, (1)*University of Texas at Austin*, (2)*The Warren Alpert Medical School of Brown University*, (3)*Women & Infants Hospital*, (4)*University of Miami*, (5)*Wayne State University*, (6)*University of Kentucky College of Medicine*, (7)*RTI International*, (8)*The University of Tennessee Health Science Center*, (9)*National Institute of Child Health & Human Development*

Background: Deficits in social attention and affective presentation are recognized features of autism spectrum disorder (ASD). However, the emergence of these social affective symptoms in infants and toddlers is poorly understood. Much of the recent research on these features in infancy

comes from studies of infant siblings of children with ASD. There is limited understanding of the emergence of ASD symptoms in the presence of other non-specific risk factors.

Objectives: To examine differences in social attention and affect in a cohort of infants later diagnosed with autism in comparison to a longitudinal cohort of babies matched on the presence of pre- and perinatal risk factors.

Methods: Subjects were recruited from the Maternal Lifestyle Study (MLS), a longitudinal investigation of the impact of prenatal substance exposure and other pre- and perinatal risk factors on infant development, including prenatal drug exposure. From the MLS (n = 1388), 11 children with ASD were identified and diagnoses were confirmed by standard methods. The ASD group was compared to a case control group matched on gestational age, presence/absence of prenatal cocaine exposure and other substances (alcohol, tobacco, marijuana; n=507). At 12 and 18 months corrected age, infants were videotaped during a standardized interaction with toys designed to assess attention, persistence, and affect in infants. Videotapes were coded for infant positive and negative affect, as well as for coordinated social attention (eye contact with the examiner) and other social communication acts defined as joint attention and behavioral requests.

Results: At 18 months, the case control group was more likely to hold up toys to show for the purpose of joint attention than was the ASD group ($p < 0.01$). Also at 18 months, the ASD group was less likely to make behavioral requests ($p < 0.01$). There were no group differences on the social attention variables between the ASD and case control groups at 12 months. There were no differences in affect displays between these groups at either age point.

Conclusions: Past research has reported diminished social attention by 12 months of age in infant siblings of children with ASD. In this study, which included infants with pre- and perinatal risk factors, we found diminished social communication at 18 months but not at the 12-month observation in children later diagnosed with autism. These findings suggest that social attention and social communication symptoms may not be reliably detected in the presence of

confounding risk factors until later points in development. An alternative explanation is that delayed development of JA in a high-risk population may diminish the specificity of this indicator in some populations. Studies using infant sibling designs require replication with alternative ascertainment methods in order to determine whether findings will generalize to the population of infants at risk for ASD. More sensitive and specific measurement tools may be needed to detect early precursor signs of autism in the context of multiple risk factors.

117.171 171 Describing the Heterogeneity of Parent-Child Dyads Including Minimally Verbal Children with Autism. S. Patterson*¹, K. Goods¹, A. P. Kaiser², R. Landa³, P. Mathy³ and C. Kasari¹, (1)University of California Los Angeles, (2)Vanderbilt University, (3)Kennedy Krieger Institute

Background: Approximately 30% of children with autism will remain minimally verbal (less than 20 spontaneous words) by school entry (Anderson et al., 2007). This population is highly heterogeneous in both cognitive and language abilities. Further, parent-child interaction appears highly varied however, dyads with minimally verbal children with ASD (mvcASD) have yet to be described. For dyads with mvcASD, supporting parents' ability to foster language building blocks including joint engagement may be essential due to the severity of children's communication delays. Learning about the ways parents engage their child with complex communication needs prior to intervention may inform the content and delivery of intervention.

Objectives: To determine reliable subgroups of parent-child dyads including mvcASD.

Methods: Participants. Participants included 59 children with autism and their primary caregivers, enrolled through a multisite intervention trial. Included children were: 1) 5- 8 years old with developmental age of at least 24 months, 2) diagnosed with autism, 3) used less than 20 words, and 4) had at least 2 years of early intervention.

Measures and outcomes. Multiple measures were taken at study entry including standardized measures of cognition (Leiter International Performance Scale: Roid & Miller, 1997) and language (Peabody Picture Vocabulary Test: Dunn & Dunn, 1995; Test of Early Language

Development: Hresko et al., 1981). Dyads were also observed during a 10-minute play interaction coded for caregivers' responsivity and directiveness (Mahoney & Perales, 2003), interaction strategies (Patterson, Goods, & Kasari, in progress), children's state of engagement from unengaged through joint engagement (Adamson et al., 2009) as well as children's initiation of joint engagement.

Results: K-means cluster analysis was conducted, identifying four unique clusters. Assessments of children's cognition and language and parental responsivity were not significantly different amongst clusters. Across clusters, significant differences were found in children's total time in each type of engagement: unengaged ($p < .03$), object engaged ($p < .01$), and joint engagement ($p < .01$) as well as parents' directiveness ($p < .01$) and appropriate use of basic interaction strategies ($p < .01$).

Four clusters were identified. Cluster one ($n=4$) included dyads with the greatest total time in child initiated joint engagement, least time unengaged with parents demonstrating greatest use of basic skills and moderate directiveness compared to other clusters. In contrast, children in cluster 2 ($n=8$) spent the least time jointly engaged, most time unengaged with parents remaining passive in the interaction. Cluster 3 ($n=32$) included children who were primarily object engaged, achieving limited time jointly engaged with moderately directive parents. Last, cluster 4 ($n=15$) described highly directive parents who spent a moderate amount of time jointly engaged with few to no child initiation of joint engagement.

Conclusions: Clusters were not defined by children's cognitive and language abilities, rather, children's state of engagement and their initiation of joint engagement significantly defined the clusters. Further parents' strategies and style of interaction also defined the clusters. However, parental responsivity was uniformly low across clusters. As such, parents' interaction style during play and the dyad's ability to enter into and maintain a joint engaged state may be key considerations for communication interventions targeting this population.

117.172 172 Associations Between Maternal Prompts and Infant Communication: Insights From the Video Diaries of Infants At Risk for Autism. M. R. Thompson*¹, C. K. Cohen¹, C. A. Nelson² and H. Tager-Flusberg¹, (1)*Boston University*, (2)*Boston Children's Hospital*

Background: Many investigators have reported that infants with increased familial risk of autism (infant siblings of children with the disorder) demonstrate significant delays and variability in their early communication abilities (see Rogers 2009 for a review). The precise nature of these language and communication delays and variable developmental trajectories in high risk infant siblings remains poorly understood. It is possible that risk status may also contribute to changes in early infant-mother dyadic interactions by altering parental behavior – either through parents' experiences with their older diagnosed child, concerns about their high risk infant, or in response to infants' emerging symptoms (Dunst, Lowe, & Bartholomew, 1990; Ozonoff et al., 2009). There is a vast literature documenting the influence of maternal language, gesture, and other communicative behaviors on the language acquisition of typically developing infants, but little is known about how these maternal factors contribute to the development of language and non-verbal communication in high risk infants (Hart & Risley, 1992; Rowe, Özçali^okan, & Goldin-Meadow, 2008).

Objectives: The goal of the current study is to examine the relationship between maternal prompts and scaffolding behaviors and infants' use of both verbal and non-verbal communication strategies during a semi-structured home-based interaction.

Methods: The current study focuses on 41 families (24 LRC, 17 HRA) participating in an ongoing longitudinal study of infants at risk for autism. As part of their participation in the larger project, families were asked to film monthly semi-structured home video diaries from 6 through 18 months. Parents were asked to complete a series of activities with their infant: presenting a variety of toys, reading a book, and engaging in social routines and interactions. During the toy exploration section, mothers are asked to hold a toy out of their infants' reach and later drop it to the floor (the 'communication probe'). The current analysis focuses on this communication probe in diaries completed between 14 and 18 months.

Tapes were scored for infants' use of gestures and other communicative strategies and for maternal communicative prompts (questions, comments, requests, and gestures). A summary score for each variable was calculated by averaging scores across the 14 – 18 month period.

Results: Families completed an average of 2.4 tapes, which did not differ by group ($t(39) = -.937, p = .36$). There were no significant group differences in the rate or type of infant communication or maternal prompts. For low risk infants, there were significant positive correlations between maternal gesture and infant gesture ($r = .46, p = .02$) and between maternal total prompts and infant directed (those that included eye contact) communicative acts ($r = .58, p < .01$). These correlations were not observed in the high risk group.

Conclusions: These findings are consistent with the previous literature on the association between maternal and infant gesture use in low risk, typically developing dyads. The implications for the high risk group are less clear, but may reflect alterations in early reciprocity. Findings for the subset who meet criteria for autism at later ages will also be discussed.

117.173 173 Brain Computer Interface (BCI) As a Potential Tool for Characterizing the Cognition of Non-Verbal Individuals with Autism. Y. S. Bonne^{*1}, J. Giron², M. Segal² and D. Friedman², (1)*University of Haifa*, (2)*Interdisciplinary Center (IDC) Herzliya*

Background: Individuals with severe autism, who do not possess functional spoken language, are often called non-verbal, but this does not necessarily imply the lack of receptive language or impaired cognition. It has been suggested that for some of these individuals, the main barrier for communication is a severe difficulty in the initiation and control of reliable intentional actions, i.e. an "output problem", and they are therefore unable to show their cognitive skills.

Objectives: Develop a brain computer interface (BCI) technique suitable for assessing the cognition of non-verbal individuals with autism, and demonstrate it at a first stage on a small group of non-autistic adults.

Methods: We have chosen an EEG-based BCI method which could be suitable for non-communicating individuals with autism as follows: (1) Steady-state visual evoked potentials (SSVEP) that allows longer presentations (e.g. 5 sec) which are less sensitive to lapses of attention or fixation than event-driven methods, with high flicker-frequency tagging (>40 Hz) that minimizes the risk for epilepsy; (2) Wide screen (~ 40 deg field-of-view, using a projector) in a dim room that minimizes distractions; (3) Presenting two or four choices, either static or moving slowly and independently around the screen to minimize spatial locking and biases typical of severe autism. We used an 8-electrode g.tec (Austria) EEG system, with a classifier first obtained by exposing the subject to simple stimuli using the minimum energy EEG method. Ten communicating adults were tested on a set of twenty 2 and 4-choice simple questions with real time feedback.

Results: There was an overall $>90\%$ matching between the answers obtained by the BCI system and the answers reported separately by the observers.

Conclusions: Our BCI method could be used to assess cognitive skills and knowledge of adult individuals, without needing explicit communication. We are currently exploring its use for characterizing the cognition of non-communicating individuals with severe autism.

117.174 174 The Relationship Between Parent-Child Dysfunction and Language Outcomes in Preschoolers with Autism. S. Druckman^{*1}, C. S. Ghilain¹, A. Gutierrez² and M. Alessandri¹, (1)*University of Miami*, (2)*Florida International University*

Background: The relationship between a parent and child is a critical variable in understanding child development. The interaction between a parent and child motivates that child to interact with their caregiver and explore their environment. It is through these positive, prosocial interactions that parents cultivate language skills and enhance overall cognitive functions (Cheung & Pomerantz 2012). It is therefore important to consider factors that can influence this relationship. One important factor affecting parent-child interactions is the mental health of the parent. Additionally, due to the core deficits in language development exhibited by children with ASD, language is an important

component of learning that is strongly affected in this population. Therefore, it is necessary to analyze the relationship between parental mental health and childhood language outcomes, in order to create the most beneficial learning environment for the child.

Objectives: The purpose of this study was to evaluate the relationship between parent characteristics and child language development. Specifically, this study investigated parent-reported depression and parent-child dysfunction, and their relationships with language functioning in preschool children with autism.

Methods: Participant data were acquired from a larger, multi-site treatment comparison study funded by the Institute of Educational Sciences (IES). Parents were asked to complete the Beck Depression Index (BDI-II) and the Parenting Stress Index – Short Form (PSI-4-SF) at the beginning (PRE) and end (POST) of the school year. Additionally, child language abilities were measured using the Preschool Language Scale, 4th edition (PLS-4) at the beginning and end of the school year.

Results: Regression analyses were conducted to evaluate the impact of parental depression and stress on their child's language scores at both PRE and POST time points. Parent-Child Dysfunction was significantly positively correlated with Parental Depression at both the PRE ($r(192) = .39, p < .01$) and POST ($r(192) = .32, p < .01$) time points.

Parent-Child dysfunction was also significantly negatively correlated with child language subscales of Auditory Comprehension, (pre - $r(192) = -.24, p < .01$, post - $r(168) = -.26, p < .01$) Expressive Communication, (pre - $r(192) = -.26, p < .01$, post - $r(168) = -.28, p < .01$) and Total Language (pre - $r(192) = -.29, p < .01$, post - $r(168) = -.27, p < .01$).

However, parental depression was not significantly correlated with child language subscales of auditory comprehension (pre - $r(193) = -.05, p < .01$, post - $r(167) = .03, p < .01$), expressive communication (pre - $r(193) = -.01,$

$p < .01$, post - $r(167) = -.02, p < .01$), and total language (pre - $r(193) = -.03, p < .01$, post - $r(167) = .00, p < .01$).

Conclusions: Preliminary analyses indicate that while depression and stress are significantly related to one another, only Parent-Child Dysfunction is negatively associated with child language outcomes. Future studies should explore whether Parent-Child Dysfunction may be influencing the relationship between parental depression and child language outcomes. These results highlight the importance of further investigating the relationship between particular aspects of parent mental health and development in children with autism.

117.175 175 Social Motivation and Its Relation to the Development of Joint Attention. J. S. Durocher^{*1}, M. N. Hale¹, A. Gutierrez², S. Novotny³ and A. M. Rowley⁴, (1)University of Miami, (2)Florida International University, (3)University of California, Davis, (4)Nova Southeastern University

Background:

Children with ASD show impairments in social functioning, most specifically in relating to others (DSM-IV-TR, APA, 2000). Researchers argue that autism may involve a failure to assign reward value to social consequences (Dube et al., 2004). Deficits in core social behaviors, such as joint attention, may therefore be secondary to a more primary disturbance in underlying social motivation mechanisms (Dawson et. al, 2005; Mundy 1995, 2003). Dube and colleagues (2004) have described a forced preference assessment for adult attention as a method for assessing social motivation, proposing that performance on this task would be related to joint attention skills. However, this relationship has not been empirically studied. Further, the construct validity of the procedure proposed by Dube and colleagues has not been systemically investigated.

Objectives:

The purpose of this study was to examine the relation between social motivation (or preference for adult attention), utilizing the procedures described in Dube et al. (2004), and joint attention skills. It was expected that these measures would be positively correlated.

Methods:

Participants included 47 children between the ages of 2 and 5. All children had a previous diagnosis of an ASD and met cutoffs for ASD or Autism on the ADOS and were part of a larger study on the effectiveness of an intervention targeting initiating joint attention skills. For the current investigation, participants were administered the *Early Social Communication Scales* (ESCS; Mundy et al., 1996, 2003) to measure joint attention, social interaction and requesting skills. A *Forced Choice Preference Assessment for Adult Attention* (FCPA-AA; Dube, 2004) was used to quantify overall levels of social motivation. During the 5-minute FCPA-AA, participants could allocate time to one of two sides of a clinic room containing either an interactive adult or an adult providing no interaction. Duration of time spent on the side of the room with the interactive adult was used as an indication of level of social motivation.

Results:

A significant positive relation was found between total initiating joint attention acts (IJA) and duration of time spent with an interactive adult during the FCPA-AA task ($r(47) = 0.288, p = 0.050$) when assessed together at an initial time point; initial FCPA-AA performance, however, was not predictive of gains in joint attention skills approximately 3 months later in a control sample ($r(12) = 0.124, p = 0.701$) or in a sample of children who were exposed to a joint attention intervention ($r(16) = -0.152, p = 0.575$).

Conclusions:

Findings suggest that the relation between social motivation and subsequent social development may be more complex than hypothesized in the literature. Specifically, data raise empirical questions regarding the methodology used to quantify social motivation and the predictive validity of the social motivation construct. Future research should aim to determine the stability of social motivation as a construct, elucidate whether individual differences in social motivation serve as a predictor of positive outcomes and response to intervention, and explore factors

which may mediate the relation between social motivation and joint attention.

117.176 176 Word Mapping Using Lexical Stress in 12-Month-Old Infant Siblings of Children with Autism and Its Relationship with Early Language Development. J. D. Ference* and S. Curtin, *University of Calgary*

Background: Typically-developing infants are highly sensitive to the rhythmic patterns of their language (Mehler, et al., 1988). This sensitivity may be directly linked to the ability to detect words in long speech streams and the learning of new words (Christophe, Mehler, & Sebastian-Galles, 2001; Curtin, et al., 2005). Indeed English-learning 12-month-olds can map trisyllabic word-object pairings with labels that differ solely in stress (STRONG-weak-weak vs. weak-STRONG-weak); Curtin, 2009). Less is known, however, about the *atypical* processing of word-stress and how this could affect early word learning. For children with Autism Spectrum Disorder (ASD), the most commonly affected aspect of speech is the production of stress, rhythm, and intonation (McCann & Peppe, 2003). Given that approximately 19% of infant siblings of children with ASD (SIBS-A) will also be diagnosed (Ozonoff et al., 2011), and that an additional 15-20% will develop language impairments (Constantino, Zhang, Frazier, Abbacchi, & Law, 2010), this population offers a unique opportunity to study possible atypical processing of word-stress and its impact on language development.

Objectives: We examined whether 12-month old SIBS-A ($n=16$) learn labels for objects (when those labels differ solely in word-stress), in the same way that typically-developing (SIBS-TD; $n=18$) 12-month old siblings do. We also examined whether this early ability was related to word comprehension at 12-months.

Methods: Infants were tested using the 'Switch task' (see Werker, et al., 1998) where they were habituated to the trisyllabic word forms 'BEdoka' and 'beDOka' (STRONG-stress denoted by capital letters) paired with novel objects that were presented on a central monitor. At test, one of the word-object pairings was mis-matched. Longer looking times to this 'switch' indicated successful mapping of the labels to the novel objects and the ability to discern minimally different word-forms. To assess early language, parents completed the

MacArthur-Bates Communicative Development Inventory (MB-CDI) (Fenson, et al., 1993).

Results: SIBS-TD looked longer to the 'switch', which was marginally significant ($p=.07$). SIBS-A infants also looked longer to the 'switch', which was significant ($p<.05$). In terms of MB-CDI scores at 12-months, SIBS-TD understood significantly more words (SIBS-TD: $M=103.72$ vs. SIBS-A: $M=51.4$; $p < .05$). A Pearson r correlation coefficient, revealed that SIBS-TD infants who looked longer during the 'switch' test trial were also more likely to understand more words at 12-months ($r=.53$, $p<.05$). For SIBS-A, there was no significant relationship between success in correctly identifying the 'switch' with the number of words understood at 12-months ($p>.05$).

Conclusions: Preliminary results indicate that both SIBS-TD and SIBS-A map word-object pairings that differ solely in stress at 12-months. Importantly, this ability was also related to early word comprehension; however, this was only true for SIBS-TD. The ability of SIBS-A to use lexical stress to map labels to objects was not obviously related to word comprehension skills at 12-months. These findings suggest that although SIBS-A may attend to lexical stress like SIBS-TD, this attention is not necessarily related to advanced language comprehension skills at 12-months as it is in typical development. A divergent path of language development for SIBS-A is therefore likely.

117.177 Assessment of Social Communication in Infants At High Risk for Autism Spectrum Disorders: Inclusion of Naturalistic Behavior Samples. M. V. Paradé*¹ and J. M. Iverson²,
(1)University of Miami, (2)University of Pittsburgh

Background: Deficits in social communication behaviors has been documented in infants and older children with ASD (e.g., Wetherby et al., 2004), and are a core feature of the disorder (DSM-IV-TR; American Psychiatric Association, 2000). Infant siblings of children with ASD are at heightened biological risk of developing ASD themselves (HR; e.g., Zwaigenbaum et al., 2009; Ozonoff et al., 2011). While symptoms of ASD are reliably measured by 18 months of age (e.g., Lord, 1995; Stone et al., 1999), a diagnosis is rarely given before the age of 2 or 3 (e.g., Turner et al. 2006). Although some argue that assessment of HR infants include natural communication samples (e.g., Tager-Flusberg et

al., 2009), very little work has followed this recommendation.

Objectives: To examine whether communicative behavior samples collected in HR infants' natural environments, in combination with commonly utilized standardized assessments, can better inform prediction of diagnostic outcome.

Methods: Fifty HR infants (44% male) were observed at home with a primary caregiver at 8, 10, 12, 14, and 18 months of age. Frequencies of infant-initiated gestures, words, non-word vocalizations, eye contact, and smiles were coded from 25-minute videotaped observations of everyday activities and parent-child toy play. At each visit, caregivers completed the MacArthur-Bates Communicative Development Inventory (CDI; Fenson et al., 2007), and infants were administered the Early Social Communication Scales (ESCS; Mundy et al., 2003). All HR infants received a diagnostic evaluation at 36 months (i.e., ADOS and clinical judgment using DSM-IV-TR criteria); nine HR infants were diagnosed with ASD (HR-ASD). Thirteen HR infants met criteria for a language delay (Language Delay; HR-LD; Heilmann et al., 2005). The remaining 28 HR infants did not meet ASD or language delay criteria (No Diagnosis; HR-ND).

Results: First, a discriminant function analysis (DFA) was run using only data gathered from the ESCS and CDI. The overall Wilks' lambda was significant, ($\Lambda = 0.50$, $\chi^2(18, N = 46) = 29.61$, $p = .041$), indicating that overall the predictors differentiated among the three groups. However, only 73.9% of the cases were correctly classified based on the ESCS and CDI scores (sensitivity = 100%, specificity = 67.6%). Next, to determine whether or not diagnostic prediction is improved by adding data gathered through natural communication samples, another DFA was conducted, adding key variables from the naturalistic observation. As before, results were significant, $\Lambda = 0.07$, $\chi^2(48, N = 46) = 81.33$, $p = .002$. However, the percentage of children correctly classified as HR-ND, HR-ASD, or HR-LD, increased from 73.9% to 93.3%. All of the HR children diagnosed with ASD at 36 months were correctly identified by the predictors in the model, yielding 100% sensitivity. Importantly, specificity (91.7%) was much improved over the previous model.

Conclusions: Overall, results demonstrated that behavior samples gathered from a naturalistic play setting improved the ability to predict whether HR infants were later classified as ASD or LD. Findings support the notion that multi-method sampling procedures that incorporate structured evaluation, parent report, and measures derived from naturalistic interactions may improve screening and diagnosis of ASD.

117.178 178 Understanding Metaphor Understanding in Autism. L. Brown*, N. Katsos and K. Plaistead Grant, *University of Cambridge*

Background:

It is often reported that even the most verbally able people with autism, i.e. those who display no deficiencies in terms of their verbal intelligence and formal linguistic knowledge, show impairments in the pragmatic use of that knowledge. Despite its prominence, the pragmatic profile in autism is relatively underexplored and not well defined or understood. Research in this area has repeatedly focused on a small range of figurative language types, with numerous studies highlighting a universal deficit in metaphor understanding.

However, despite the vast literature surrounding metaphor typology, relating it to conceptual development and noting it as a key factor affecting metaphor comprehension, in research examining individuals with ASD, these differences between metaphor have received little and inconsistent attention.

Objectives:

To critically review and expand on the understanding of metaphor comprehension in ASD, particularly by acknowledging and incorporating more linguistic literature regarding metaphor typology and assessment. We aim to link psychological and linguistic explanations and address why this is important.

Methods:

We present a critical overview and analysis of current literature addressing metaphoric comprehension in autism spectrum disorders,

approached from both psychological and linguistic perspectives.

Results:

From reviewing recent studies, across multiple sites, using diverse methods, and participants of different autism subtypes, ages, and cognitive levels, it appears difficult to assert any systematic comparison in metaphoric comprehension ability in ASD. Further inconsistencies in linguistic definitions of metaphor typology and assessment tasks and methods result in varying metaphoric comprehension ability profiles. Wider analysis of current literature will be presented.

Conclusions:

To advance the field, experimental measures will benefit from a more interdisciplinary approach; combining psychological and linguistic explanations and methodologies may offer more systematic explanation of the pragmatic difficulties in this population. The implementation of combining these experimental frameworks will be discussed.

Keynote Address Program

118 Advances in Autism: Genetics Filling the Empty Fortress

Genetics has revolutionized the conceptualization of autism, and promises rationale, mechanistically based therapeutics in the future. At the same time, as our genetic understanding of ASD etiology advances, we must first tackle extraordinary complexity at multiple biological levels, from molecules to cells to circuits and behavior. Recent work in the genetics of ASD predicts that about 1000 genes contribute to the overall population risk for ASD. Furthermore, no major effect gene accounts for more than 1% of cases. Genetic effect sizes range from very small (for common variants), to rare mutations that are essentially considered causal. However, even for the most major, causal mutations, the effects appear to extend across current disease boundaries. These data have challenged our lab to focus on two major questions: understanding what are the neurobiological consequences of ASD risk mutations and whether there are common or convergent molecular mechanisms that link ASD cases with diverse etiologies. I will discuss our work using genetically based animal and in vitro models to understand ASD pathophysiology, as well as our work using systems biology approaches and network inference to connect multiple levels of biology in a coherent manner. Our work in transcriptional profiling reveals strong evidence of convergence on common pathways in the ASD post mortem brain. Overall, these data and that of others support the existence of convergent molecular pathways in ASD. Using this information to develop novel

therapeutics in children and adults with ASD remains a critical challenge.

118.001 Advances in Autism: Genetics Filling the Empty Fortress. D. H. Geschwind*, *University of California at Los Angeles*

Genetics has revolutionized the conceptualization of autism, and promises rationale, mechanistically based therapeutics in the future. At the same time, as our genetic understanding of ASD etiology advances, we must first tackle extraordinary complexity at multiple biological levels, from molecules to cells to circuits and behavior. Recent work in the genetics of ASD predicts that about 1000 genes contribute to the overall population risk for ASD. Furthermore, no major effect gene accounts for more than 1% of cases. Genetic effect sizes range from very small (for common variants), to rare mutations that are essentially considered causal. However, even for the most major, causal mutations, the effects appear to extend across current disease boundaries. These data have challenged our lab to focus on two major questions: understanding what are the neurobiological consequences of ASD risk mutations and whether there are common or convergent molecular mechanisms that link ASD cases with diverse etiologies. I will discuss our work using genetically based animal and in vitro models to understand ASD pathophysiology, as well as our work using systems biology approaches and network inference to connect multiple levels of biology in a coherent manner. Our work in transcriptional profiling reveals strong evidence of convergence on common pathways in the ASD post mortem brain. Overall, these data and that of others support the existence of convergent molecular pathways in ASD. Using this information to develop novel therapeutics in children and adults with ASD remains a critical challenge.

119 The Role of Environmental Exposures in Autism Etiology: A Retrospective of the Last Decade, New Results and Frontiers for the Future

Moderator: I. Hertz-Picciotto *UC Davis M.I.N.D. Institute*

Organizer: I. Hertz-Picciotto *University of California Davis*

The last decade has witnessed the rapid growth of a body of literature on environmental factors that alter risk for autism. Air pollution, household products, nutrition, maternal obstetric factors, medical interventions and medications, and infections have featured prominently, with particular focus on prenatal influences. This symposium will summarize the state-of-the-science 10 years ago, when few non-genetic etiologic clues had been uncovered. The bulk of

the symposium will be devoted to describing major developments in methodology and results since then, providing depth on four classes of exogenous chemical and microbiologic exposures during gestation: air pollution, pesticides, nutrition, and infections. Dr. Marc Weisskopf will address what has been learned about air pollution, the challenges and advances in exposure assessment, recent convergent findings from multiple independent studies in different regions of the U.S. He will then present a novel analysis based on linking EPA modeled pollutant levels to residences near the time of birth of children born to Nurses Health Study-2 participants, including those with and without autism. Dr. Irva Hertz-Picciotto will summarize published and new evidence about insecticides, commonplace chemicals that are perhaps unique in having been designed specifically to damage living organisms. Potential mechanisms of neurotoxicity will be discussed along with epidemiologic studies covering both commercial (largely agricultural) and household applications of organochlorines, organophosphates, and pyrethroids, including new analyses from the CHARGE (CHildhood Autism Risks from Genes and Environment) Study. Dr. Rebecca Schmidt will describe the literature on maternal nutritional status in relation to autism, including several publications indicating a protective role of folate in the periconception, present evidence for gene-by-environment interactions with relatively common polymorphisms in the one-carbon metabolism pathway, and then report new data on prenatal iron status. Other aspects of diet will be touched on, and potential mechanisms such as a role for epigenetic alterations will also be discussed. Dr. Hjordis Atladottir will provide an overview of maternal infection and inflammation in autism etiology, beginning with possibly the earliest identified environmental factor, rubella, and tracing recent work on microbial exposures and inflammatory markers. This critical review will cover both epidemiologic and experimental results, characterize the methodologic limitations and pitfalls in work to date, and highlight where further work is needed. Together these four presentations will review our current knowledge base in regard to these four ubiquitous exposures, place this work in the context of the maternal-fetal interface, explain where the research is leading, highlight the challenges, and point to the directions that appear to be the most promising.

119.001 Perinatal Air Pollution Exposure and Autism, with New Results in the Nurses' Health Study-2. A. L. Roberts¹, K. Lyall², F. Laden¹, J. Hart³, A. C. Just¹, K. Koenen⁴, A. Ascherio¹ and M. G. Weisskopf*¹, (1)*Harvard School of Public Health*, (2)*UC Davis M.I.N.D. Institute*, (3)*Brigham and Women's Hospital*, (4)*Columbia University Mailman School of Public Health*

Background: Over the past several years, research into environmental toxicants as possible risk factors for autism has made steady progress. We review this progress with respect to metals and other air pollutants, beginning with early suggestive findings from methodologically weak studies that utilized exposure measures made after diagnosis or that recruited potentially biased samples of cases and controls. We trace the improvements in exposure assessment and study

design, such as the use of county level mercury releases in an ecologic study in Texas to estimate exposure independently from autism, to the use of air pollutant exposure models or distance to road as a proxy for traffic-related pollutants in individual-level studies. This emerging evidence points to a possible association between perinatal exposure to hazardous air pollutants and autism.

Objectives: To examine the association between perinatal exposure to air pollution and risk of autism spectrum disorder in a large national cohort, building upon the advances made in previous work.

Methods: We used logistic regression to estimate odds ratios and 95% confidence intervals (CI) for the association between U.S. Environmental Protection Agency modeled levels of hazardous air pollutants at the time and place of birth and risk of autism in the children of mothers in the Nurses' Health Study II, which includes women from across the entire United States (cases=325; controls=22,120). Our analyses focused on pollutants associated with autism in prior research. We adjusted for possible ascertainment bias by both family-level socioeconomic status (e.g., income, partner's education, maternal grandparents' education) and census-tract-level socioeconomic measures (e.g., tract median income, percent college educated). We also examined possible differences in the relationship between autism and pollutant exposure by child's sex. We ran multi-pollutant models and explored the novel statistical approach of random forests to try to identify particular toxicants responsible for associations among many correlated exposures.

Results: Perinatal exposure to higher levels of diesel, lead, manganese, mercury, methylene chloride, and a combined measure of metals were linearly related to increased risk of autism ($p < .05$ for each). These associations persisted only among boys in analyses stratified by sex. Odds ratios for autism in boys in the highest versus lowest quintile of exposure to these pollutants were 1.72 (95% CI: 1.15-2.56) for lead, 1.52 (95% CI: 1.03-2.23) for manganese, 1.91 (1.11-3.28) for mercury, 2.23 for diesel (95% CI: 1.03-4.81), and 1.82 (95% CI: 1.19-2.79) for methylene chloride. Multi-pollutant models suggested mercury and methylene chloride to be the most robustly associated with autism. Random

forests suggested exposure to arsenic, mercury, chromium, trichloroethylene, and manganese as most important predictors of autism status.

Conclusions: Gestational exposure to air pollution may increase risk for autism. Exposure to metals and other air pollutants have known effects on the immune system, can dysregulate calcium processes in the brain, and can be directly neurotoxic. Such mechanisms could underlie the association between these pollutants and autism. Methodological challenges persist, though, in determining which toxicant(s) among many correlated ones are causal factors.

119.002 Evidence for Gestational Nutrition Influences On Autism Risk, with New Findings for Iron. R. J. Schmidt*, *UC Davis MIND Institute*

Background: Gestational nutrition is known to influence child cognition and behavior due to the influence, during critical time windows, of nutrients such as folate, other B-vitamins, and iron, on brain, spinal cord, and neuron development. Evidence is building for a role of gestational nutrition in the etiology of autism spectrum disorders (ASD).

Objectives: To review the research to date on the role of gestational nutrition in relation to risk for ASD in the child, discuss potential mechanisms, and present new findings in the CHARGE (Childhood Autism Risks from Genetics and Environment) case-control study on supplemental iron.

Methods: Children with a diagnosis of ASD or typical development (TD) confirmed at the UC Davis MIND Institute using standardized clinical assessments were included. We collected through structured telephone interviews maternal intake of multivitamins, prenatal vitamins, nutrient-specific vitamins, cereals, and other supplements for the three months before pregnancy, each month of pregnancy, and during breastfeeding (the index period). Data included whether or not each item was consumed, and if so, the brand, dose, frequency and months consumed. From this information, for each woman we calculated a total average value of selected nutrients (including iron) for each month.

Results: Mothers of children with ASD were significantly less likely than mothers of TD children to report taking an iron supplement at any point during the index period before and after adjustment for folic acid, maternal education, and child's year of birth (odds ratio=0.7, 95% confidence interval: 0.5, 0.9, $P=.015$). Iron supplements were reported more often during the second and third trimesters, and lower use of iron supplements by ASD mothers during this time was driving the difference between case and control mothers observed for the index period. In addition, log-transformed mean (SD) total daily iron intake quantified from all sources for the index period was lower for mothers of children with ASD (3.7 (0.7) mg/d) than for mothers of children with TD (3.9 (0.7) mg/d, $p=0.01$), and ASD risk declined as iron increased ($P_{\text{trend}}=0.01$).

Conclusions: Evidence for a role of nutrition in ASD etiology is similar to that observed for other neurodevelopmental conditions. Maternal folic acid intake near conception was associated with decreased risk for ASD, especially in those genetically susceptible to inefficient metabolism. Though few women in the US are expected to be deficient in folate, supplemental folic acid could compensate for metabolic insufficiencies or increased demands. In the case of iron, supplementation is more likely to be compensating for deficiencies. Iron deficiency affects 40-50% of pregnant women and can induce fetal iron deficiency because maternal circulation constitutes the only source of iron to the developing fetus. Like other nutrients, iron plays a crucial role in early neurological development, and deficiencies early in life result in impaired cognition, motor development, social orientation and engagement, and language development. In the brain, iron contributes to neurotransmitter production, myelination, and immune function; dysregulation of all three of these pathways have been associated with ASD. Further investigations of nutritional contributions to ASD are needed to identify strategies for prevention.

119.003 Insecticides and Risk for Autism: Overview and New Results From the CHARGE Study. I. Hertz-Picciotto*¹, L. Delwiche², F. Tassone¹, D. Bennett², D. J. Tancredi³, R. Hansen⁴, S. Ozonoff¹ and I. N. Pessah¹, (1)UC Davis M.I.N.D. Institute, (2)UC Davis, (3)UC Davis School of Medicine, (4)The M.I.N.D. Institute, University of California, Davis

Background: Insecticides are designed to damage living organisms, often by targeting the CNS. Several recent studies have provided evidence of a link between specific classes of pesticides and the risk for autism or for symptoms of pervasive developmental disorders (PDD). These used objective measures of exposure: one linked commercial applications of organochlorine, pyrethroid, and other pesticides from a statewide database to residences during pregnancy; a second attempted to replicate those findings in a sample of cases and controls with more detailed confounding information; a third measured urinary metabolites of organophosphates during pregnancy and followed the children, obtaining the PDD measures through the Child Behavior Checklist.

Objectives: 1) To examine the relationship of autism spectrum disorder (ASD) risk with household applications of insecticide products and specific active ingredients in those formulations. 2) To evaluate evidence for an interaction between pyrethroid exposures and MAOA genotype.

Methods: Participants (n=783) were enrolled in the Childhood Autism Risks from Genes and Environment (CHARGE) study beginning in 2003. ASD was confirmed on the ADOS and ADI-R. Controls were recruited from State birth files, using a stratified random sample matched on age, sex, and broad geographic area, and were considered typically developing (TD) if they scored higher than 2 SD below the mean on Mullen's Scales of Early Learning and Vineland Adaptive Behavior Scales, and below 15 on the Social Communications Questionnaire. Exposures to household products were collected through an extensive interview that obtained product type, use and brand, and associated time periods of use from preconception through pregnancy and early childhood. Insecticides were searched in online databases (http://www.pesticideinfo.org/Search_Products.jsp, <http://www.epa.gov/oppsrrd1/reevaluation/pyrethroids-pyrethrins.html>) containing active ingredients by brand, type, and date to assign specific chemical exposures. Standard PCR was used for genotyping the variable number tandem repeats in the promoter region of the X-linked MAOA gene.

Results: Parents of ASD children were more likely than those of controls to report applications of insecticide sprays and foggers in the preconception and pregnancy period, and the products they used were more likely to contain pyrethroids (multivariate adjusted Odds Ratio, aOR=1.88 (95% confidence interval (CI), 1.21, 2.94)). Repeated applications (6 or more months during pregnancy) conferred especially high risk (aOR=3.47, 95% CI=1.48, 8.11). Boys carrying four tandem repeats in the MAOA promoter locus, were at exceptionally high risk (nearly five-fold) if pyrethroids were used. Products containing less toxic pyrethrins carried lower risks, and results were robust to various sensitivity analyses.

Conclusions: Reporting accuracy could differ for mothers of ASD versus unaffected children, but the synergistic relationship for pyrethroid use and MAOA genotype is incompatible with this explanation. Moreover, participants reported products they used, not exposures: the latter were determined by linkage of product type, brand, and year of use with databases providing active ingredients; these often changed over time. Evidence presented here suggests the pyrethroid class of insecticides comprise a modifiable environmental factor that may increase ASD risk, particularly in genetically susceptible individuals, but replication in a prospective setting should be sought.

119.004 Role of Infection and Immune Activation During Pregnancy in the Etiology of Autism. H. O. Atladottir*, *University of Aarhus*

Background: An increasing number of scientific papers have suggested that maternal infection and maternal immune activation during pregnancy are associated with the development of autism. The literature in the field has increased extensively during the last decade and includes case reports, studies on inflammatory markers in humans, animal experimental studies, and epidemiological studies.

Objectives: The main purpose of this presentation is to give a brief overview of the scientific literature concerning infection and maternal immune activation and the development of autism. Potential mechanisms on how maternal infection and maternal immune activation can be etiologically associated to the development of autism will be described. Findings from

epidemiological studies will be discussed in the light of results from case reports and animal studies.

Methods: The presentation includes a systematic walk-through of important scientific findings published during the last decade concerning infections and immune activation during pregnancy and development of autism. The audience will get an overall view of the literature with focus on consistency in findings. The strengths and limitations of especially epidemiological research will be discussed as well as the importance of cautious interpretation of results from epidemiological studies.

Results: Early case reports and comparative studies have suggested maternal prenatal viral infections to be associated with the development of ASD. Results from recent animal studies suggest that infection-induced maternal immune activation leads to a fetal inflammatory response that has been implicated in the development of autism. However, the picture is still incomplete, and data mostly experimental. Only few epidemiological studies have investigated the association between specific infectious diseases in pregnancy and development of autism. These epidemiological studies have had methodological limitations, such as limited completeness and validity of exposure data. While not definitive, the findings have been suggestive of a link.

Conclusions: Infection and immune activation during pregnancy is possibly an important etiological factor in the development of autism in certain individuals. Future research will most likely continue to focus on how specific immunological reactions during pregnancy are associated with autism, and with time research will presumably focus more on the interaction between genetics and immune system insults. Future epidemiological studies can benefit from validated data on infectious exposure. Whenever possible, scientists doing autism research should consider including other neurodevelopmental outcomes in order to explore the autism specificity of their results.

Cell Biology Program
120 Cell Biological Mechanisms

This session presents abstracts on cellular mechanisms that may contribute to the autism phenotype including those defined in induced human progenitor cell lines, brain tissue, peripheral blood and genetic neuronal models.

120.001 Generation and Neuronal Differentiation of Self-Renewing Neuronal Progenitor Cell Lines As a Model to Investigate Synaptic Development and Functions in Patients Affected by the Phelan-Mcdermid Syndrome (PMS). D. I. Orellana*¹, E. Faggiani¹, E. Fusar Poli², L. Carlessi², G. Bechi¹, C. Vicidomini³, C. Sala³ and C. Verpelli³, (1)Neurological Institute Foundation Carlo Besta, (2)Fondazione IRCCS Istituto Nazionale dei Tumori, (3)CNR Institute of Neuroscience

Background:

Phelan-McDermid syndrome is a developmental disorder characterized by severe expressive language and speech delay, hypotonia, global developmental delay, and autistic behaviour. Haploinsufficiency of the SHANK3/PROSAP2 gene is very likely to be an essential cause of the major neurological features associated with PMS. Shank3 is a large scaffolding protein enriched in the postsynaptic density (PSD) of neuronal synapses. When expressed in cultured hippocampal neurons, Shank3 promotes the maturation and enlargement of dendritic spines while Shank3 mouse mutants showed altered PSD protein composition, reduced size of dendritic spines and weaker basal synaptic transmission. Neuronal progenitor cell derived from human Induced pluripotent stem (iPS) represent an accessible and expandable source of disease specific cell types, offering an opportunity to study neuronal development and degeneration, circuit formation and function, and for generating new *in vitro* human models of brain diseases.

Objectives:

Generation and neuronal differentiation of self-renewing neuronal progenitor lines obtained from PMS patients and age-matched healthy individuals' iPS cells (PMS-NP cells) to study the role of Shank3 in synapse formation and function.

Methods:

Fibroblasts from different affected children with the PMS were reprogrammed to iPS cells using the hSTEMCCA-loxP lentivirus. iPS cells were differentiate until obtain self-renewal human neuronal precursors (hNPs) from wild type and

disease-related hiPSCs. hNPs were differentiated into functional cortical neurons through three different protocols: by coculturing them with rat primary neurons; glial cells; or simply by culturing them on matrigel.

Results:

The hNPs did not express markers of pluripotency such as OCT 3/4 and Tra-1-81 while expressing Nestin, which was progressively lost following the induction of terminal differentiation. The expression of Nestin however was maintained for up to 20 passages in all hNP cells. About 50% of the cells were also positive for the neuronal marker Tuj1 and only a minority of them was positive for the glial marker GFAP. We analyzed neuronal differentiation by using MAP2 for labeling dendrites, and VGLUT1 along with Synaptophysin for labeling synapses. hNP-derived neurons had elaborate dendritic arbors and many Synaptophysin-positive puncta. VGLUT1 positive puncta were detected starting around day 50 of differentiation. We observed that the majority of the neurons generated from hNP cell cultures were MAP2+/VGLUT1+ excitatory neurons, and we basically did not detect MAP2+/GABA+ cells. However, after 60 days of differentiation of treated co-culture with 1µM retinoic acid, we detected GABAergic neurons and observed a MAP2+/GAD67+ population of cells. Additionally, hNP from patients affected by PMS presented a reduction in the levels of Shank3 compared to controls subjects.

Conclusions:

Here we describe the establishment of replicating neuronal-committed stem cell lines from human iPSCs. These cells can self-renew and specifically generate neuronal lineages that can be differentiated into mature neurons using different methodologies. This model presents a valuable approach to study PMS.

120.002 Redox-Sensitive Protein Dynamics in Lymphoblastoid Cell Lines From Patients with Autism Spectrum Disorders. A. Chiochetti¹, D. Haslinger¹, T. Karl¹, S. Wiemann², C. M. Freitag³, F. Poustka³, B. Scheibe¹, J. Bauer⁴, H. Hintner⁴, M. Breitenbach¹, J. Kellermann⁵, F. Lottspeich⁵, S. M. Klauck*² and H. Breitenbach-Koller¹, (1)University of Salzburg, (2)Deutsches Krebsforschungszentrum (DKFZ), (3)Goethe

Background:

Autism spectrum disorders (ASD) are characterized by inheritance of heterogeneous genetic risk factors proposed to cause the specific neurologic behavioural phenotype. The cellular correlates dysfunctional in ASD are targeted by pathways of neurogenesis and synaptic plasticity. In addition, biological networks such as energy metabolism and oxidative stress seem to be disturbed at the cellular level.

Objectives:

To distinguish between general ASD-specific and individual patient-specific cellular network perturbations we employed proteomic studies on lymphoblastoid cell lines (LCL) established from patients with a known mutation in the ribosomal protein L10 gene (*RPL10*) and a set of patients without any *RPL10* mutation. This approach would report on protein expression patterns and consequently on functional pathways involved in the pathophysiology of ASD patients with different genetic backgrounds.

Methods:

In this study we applied 2D-differential-in-gel-electrophoresis (2D-DIGE) coupled with tandem mass spectrometry (MS/MS) to analyze the overall protein expression pattern in individual LCLs. Validation of differentially regulated proteins was performed at mRNA and protein expression level using qRT-PCR and Western Blot methods. We studied LCLs from members of two independent families carrying a RPL10-H213Q mutation in comparison to a non-mutation carrier of one family and healthy controls. To investigate if similar differentially regulated protein patterns could be observed in the general ASD population we analyzed a distinct set of 10 ASD patients not harbouring any RPL10 mutation in comparison with 10 random controls. A yeast model system was employed to validate and compare in wild-type and RPL10-deficient cells, respectively, a possible oxidative stress effect on protein expression.

Results:

In the RPL10 mutation analysis we discovered alterations in the expression level of different protein isoforms operative in glycolysis/energy metabolism (TPI1 and GAPDH), oxidative stress (ECH1) and mRNA regulation (HNRNPK). Then, in the additional set of LCLs from ASD patients who do not carry a RPL10 mutation we identified 19 differentially expressed candidates. These 19 proteins map to energy metabolism, mRNA and protein metabolism, cytoskeleton, and redox regulation. Therefore, the proteome profile of both experimental ASD groups overlap in energy metabolism and oxidative stress response, but with different protein representatives. Interestingly, most of the candidates have been previously described as redox-sensitive. Furthermore, the RPL10-deficient yeast cells under standard conditions show a subset of differentially expressed proteins that are observed in wild-type cells only under oxidative stress, and these again mapped to energy metabolism and oxidative stress response.

Conclusions:

We conclude that there is a redox-sensitive cellular response under conditions of RPL10 deficiency, which is part of an altered protein expression profile observed in the general ASD patient set. Of note, dysfunctions of energy metabolism and oxidative stress regulation as implicated by our results may be tolerated in LCLs, but be more deleterious in neuronal cells by causing a detrimental redox imbalance under the high oxygen pressure of neural cells. Thus, imbalance in energy/redox metabolism or a redox-sensitive dysfunction may lead to altered processes of neuronal development or function causing the ASD phenotype.

120.003 Increased Susceptibility of Autism Lymphoblastoid Cells to Mitochondrial Dysfunction Following Reactive Oxygen Species Challenge. S. Rose^{*1}, R. E. Frye², S. Melnyk¹, R. A. Wynne³ and S. J. James¹, (1)University of Arkansas for Medical Sciences, (2)Arkansas Children's Hospital Research Institute, (3)Arkansas Children's Hospital

Background:

Despite being one of the most prevalent metabolic abnormalities affecting children with autism spectrum disorders (ASD), the significance of mitochondrial dysfunction in ASD remains poorly understood. We and others have previously

demonstrated that many children with ASD exhibit elevated oxidative stress markers. In addition, we have shown a reduction in glutathione-mediated redox capacity in plasma, primary immune cells, as well as lymphoblastoid cell lines (LCLs) and mitochondria isolated from LCLs derived from children with ASD. Autism LCLs produce significantly more reactive oxygen species (ROS) and exhibit an increased susceptibility to mitochondrial membrane depolarization following acute nitric oxide exposure relative to control LCLs. This evidence suggests that glutathione-mediated redox capacity is insufficient to counter endogenous ROS production in ASD LCLs resulting in increased vulnerability to oxidative damage and mitochondrial dysfunction during pro-oxidant exposures.

Objectives:

We sought to determine whether decreased glutathione-mediated redox capacity in ASD LCLs renders them more susceptible than control LCLs to mitochondrial dysfunction following acute oxidant exposure and whether pretreatment to increase the intracellular glutathione concentration would confer protection from mitochondrial dysfunction.

Methods:

Mitochondrial function was measured in intact LCLs in real-time using Seahorse extracellular flux (XF) technology. The oxygen consumption rate (OCR) at baseline (Basal OCR) and upon the sequential addition of mitochondrial inhibitors was measured and a bioenergetic profile was derived from these measurements. We compared bioenergetic profiles from 15 ASD and control LCLs before and after a 1 h exposure to 5-15 μM DMNQ (2,3-dimethoxy-1,4-naphthoquinone), a ROS generator. To determine whether changes in mitochondrial bioenergetics after DMNQ exposure could be prevented by NAC-induced increases in the intracellular glutathione redox capacity, a third comparison group consisted of the ASD LCLs pretreated for 48 h with 1 mM N-acetyl-cysteine (NAC). In addition, the intracellular glutathione redox capacity in ASD and control LCLs was measured by HPLC, and the mitochondrial to nuclear DNA ratios (mtDNA/nDNA) were determined.

Results:

At baseline (i.e. no DMNQ challenge), ASD LCLs exhibited a significantly increased mitochondrial Reserve Capacity (Maximal OCR- Basal OCR) relative to controls ($p=0.04$). Challenge with DMNQ resulted in significantly higher Basal OCR (10-15 μM ; $p\leq 0.04$), Proton Leak (5-10 μM ; $p\leq 0.03$), and a greater depletion of Reserve Capacity (10-15 μM ; $p\leq 0.03$) in ASD LCLs relative to control LCLs. NAC pretreatment of the ASD LCLs successfully increased the intracellular glutathione-mediated redox capacity ($p<0.001$) and attenuated the abnormal depletion of Reserve Capacity observed with DMNQ challenge relative to control LCLs. The average mtDNA to nDNA ratio was significantly lower in the ASD LCLs relative to control LCLs ($p<0.01$).

Conclusions:

We demonstrate that acute exposure to a ROS-producing agent results in a detrimental effect on mitochondrial bioenergetics that is greater for ASD LCLs as compared to control LCLs. Further, targeted treatment to restore intracellular glutathione redox capacity improves the ability of the ASD LCLs to withstand excessive ROS exposure. The increased mitochondrial Reserve Capacity of the ASD LCLs is likely an adaptive response to chronic oxidative stress and initial studies indicate that increase Reserve Capacity is not due to increased numbers of mitochondria.

120.004 Reduced Activities of Mitochondrial Electron Transfer Chain Complexes and Pyruvate Dehydrogenase in the Frontal Cerebral Cortex in Autism. A. Chauhan*¹, F. Gu¹ and V. Chauhan², (1)*NYS Institute for Basic Research in Developmental Disabilities*, (2)*NYS Institute for Basic Research In Developmental Disabilities*

Background: The cause of autism is elusive but accumulating evidence from our and other groups suggests mitochondrial dysfunction and oxidative stress in autism. Mitochondria electron transport chain (ETC) consists of five multi-subunit enzymes, i.e., complex I-V, which differs not only in structure but also in function, and plays an important role in energy, i.e. adenosine triphosphate (ATP) generation. ETC also generates most of the endogenous free radicals, i.e., reactive oxygen species (ROS) of the cell. Pyruvate dehydrogenase (PDH) is the key regulatory enzyme of cellular metabolism and is

localized in the mitochondrial matrix. It links the tricarboxylic acid cycle and subsequent oxidative phosphorylation by the mitochondria with glycolysis and gluconeogenesis as well as with lipid and amino acid metabolism.

Objectives: Recently, we reported brain region-specific deficit in the protein expression of mitochondrial ETC complexes in the cerebellum and cortices from frontal and temporal regions from the children with autism. The aim of this study was to compare the activities of mitochondrial ETC complexes and PDH enzyme in the frontal cerebral cortex from subjects with autism and age-matched controls.

Methods: Frozen human brain tissues (frontal cerebral cortex) of autistic and age-matched control subjects were obtained from the NICHD Brain and Tissue Bank for Developmental Disorders at the University of Maryland. Mitochondria were isolated from frontal cortex tissues according to the differential centrifugation method. Protein concentrations of mitochondria in samples were estimated by bicinchoninic acid protein assay kit. The activities of mitochondrial ETC complexes I, II, III, IV, V, and PDH enzyme were analyzed using microplate assay kits.

Results: The results showed deficiencies of activities of ETC complexes I and V to be most prevalent in autism that was observed in 43% of autism subjects, followed by deficiency in activity of complex III in 29% and of complexes II and IV in 14% of autistic subjects when compared with control group. Multiple deficiencies of ETC complexes were observed in 29 % of autistic subjects. PDH activity was also significantly reduced in 57% of autistic subjects as compared to control group.

Conclusions: These results suggest that autism is associated with mitochondrial abnormalities in the brain that may lead to oxidative stress and abnormal energy metabolism.

120.005 Oxidative Stress Markers in Children with Autism Spectrum Disorders. M. E. Gonzalez Fraguera*, *International Center for Neurological Restoration*

Background: The etiology of autism spectrum disorders (ASD) remains elusive, this medical condition is considered a multifactorial disorder

influenced by genetic and environmental factors as well as increased vulnerability to oxidative stress. The understanding of the potential role of oxidative stress in the etiopathogenesis of autism would be very useful for earlier clinical, therapeutic or preventive strategies.

Objectives: To evaluate the redox status in ASD patients compared with control children.

Methods: To evaluate the redox status we quantified the activity of the antioxidant enzyme catalase (CAT), glutathione concentration (GSH) and markers of damage to biomolecules, malonyldialdehyde (MDA) and 8-hydroxy-2deoxyguanosine (8OHdG) in peripheral blood samples of 45 children with autism and 42 age-matching control children.

Results: The reduced GSH content in autistic patients was significantly lower compared with the control group (0.24 ± 0.162 vs. 0.94 ± 0.115 , respectively, $p \leq 0.001$). Higher serum CAT, MDA and 8OHdG levels were found in children with autism compared with controls (CAT, 2.836 ± 0.479 vs. 0.689 ± 0.157 , $p \leq 0.001$; MDA 8.6 ± 0.5 vs. 1.76 ± 0.33 $p \leq 0.001$, and 8OHdG 13.134 ± 1.33 vs. 1.46 ± 0.326 , $p \leq 0.001$).

Conclusions: The present study supports the notion that oxidative stress is associated with autism, but additional researches are needed to investigate how it may contribute to autistic pathophysiology and these studies are currently in progress.

120.006 JAKMIP1 Is a Novel Component of an FMRP-Associated RNP Complex and Regulates Neuronal Translation. J. M. Berg*¹, L. Chen¹, A. Oguro-Ando², J. L. Stein¹, J. A. Miller¹, A. A. Vashisht¹, E. P. Kite¹, A. Li¹, O. Penagarikano³, J. A. Wohlschlegel¹ and D. H. Geschwind³, (1)*The University of California, Los Angeles*, (2)*UCLA*, (3)*University of California at Los Angeles*

Background : The regulation of neuronal translation is crucial for proper neuronal development and function and is among several biological processes implicated in autism spectrum disorders (ASD). Janus kinase and microtubule-interacting protein 1 (JAKMIP1) is dysregulated in ASD subjects with Fragile X syndrome, (dup)15q, and idiopathic ASD. However, its role in brain development is unknown.

Objectives: We used an unbiased approach to characterize JAKMIP1's protein interactome. We identified an interaction with the FMRP-associated translational complex and are interested in the mechanism and purpose of the FMRP-JAKMIP1 interaction, JAKMIP1's association and regulation of FMRP mRNA translational targets, and JAKMIP1's role in neuronal translation.

Methods : We used Multidimensional Protein Identification Technology (MudPIT) to identify JAKMIP1's proteomic interactome. To test JAKMIP1's presence in polyribosomes, we conducted polyribosome fractionation, immunoprecipitation from a BacTRAP neural cell line expressing eGFP-tagged polyribosomes, and immunocytochemistry of JAKMIP1 and poly(A)-binding protein 1 (PABPC1) in neurons. To test JAKMIP1's association with FMRP mRNA targets, we conducted quantitative RTPCR with RNA from JAKMIP1 immunoprecipitation. We tested JAKMIP1's translational control of a subset of these targets by protein analysis at synaptosomal membranes in neural systems with reduced JAKMIP1. We used fluorescence non-canonical amino acid tagging (FUNCAT) to assess translation in neurons lacking JAKMIP1.

Results: We show that JAKMIP1 is present in the polyribosome fraction and binds FMRP protein as well as several of its mRNA targets, including *Fmr1* and *PSD95*, both of which have increased expression in synaptosomal membranes upon *Jakmip1* knockdown. Furthermore, we show that neurons from *Jakmip1* knockout mice show significantly reduced nascent translation.

Conclusions : These results identify JAKMIP1 as a new protein involved in the regulation of neuronal translation and show that it interacts with the process of FMRP-related translational control. Elucidation of the precise molecular interactions occurring within the JAKMIP1 and FMRP-associated complex, its relationship to neuronal activity, as well as the interaction of JAKMIP1 with the transport machinery are exciting new directions that we are exploring.

H. Ropers⁶, M. Raynaud², A. Toutain² and F. Laumonier*¹,
(1)*Inserm UMR930*, (2)*Centre Hospitalier Regional Universitaire*, (3)*Radboud University Medical Centre*, (4)*Institut Cochin*, (5)*UZ Leuven*, (6)*Max Planck Institute for molecular genetics*

Background: The *PTCHD1* gene (Patched Homology domain 1), located at Xp22.1, has been recently involved in studies describing genomic deletions and missense mutations in patients with autism and/or non-syndromic intellectual disability (ID).

Objectives: Considering that this gene represent a strong candidate for these neurodevelopmental disorders, we searched for mutations on genomic DNA of patients and families collected from the EuroMRX consortium cohort.

Methods: The *PTCHD1* gene was sequenced in 400 families with autism and/or ID. We also performed neurodevelopmental expression and neuronal subcellular localization studies in mouse brain: the neurodevelopmental expression profile of the mouse *Ptchd1* gene was assessed in brain tissues at different developmental stages (in vivo analysis) and in primary neuronal cultures (in vitro). The neuronal subcellular localization was performed by immunocytochemistry analyses on mature primary neuronal cultures using a custom *PTCHD1* antibody, and by transfection experiments using GFP tagged *PTCHD1*.

Results: We characterized a point deletion in the *PTCHD1* gene coding sequence (c.2128delC, p.L710CfsX12), which would lead to the expression of a truncated form of the *PTCHD1* protein lacking the last 180 amino-acids, in a French family with non-syndromic ID and autism. Little is known regarding the neurodevelopmental expression of the *PTCHD1* gene, as well as the neuronal function of the encoded protein. Immunocytochemistry analyses on mature primary neuronal cultures using a custom *PTCHD1* antibody revealed that *PTCHD1* transmembrane protein co-localized with postsynaptic inhibitory (Gephyrin) and excitatory (*SHANK3*) markers. We also showed that the C-terminal intracellular tail of *PTCHD1* was essential for dendrite targeting. Interestingly, the protein sequence indicate that the last 4 amino-acids (ITTV) fit with a PDZ binding domain consensus sequence that is found in various postsynaptic

120.007 Mutation of the *PTCHD1* Gene, Which Encodes a Transmembrane Protein Expressed in Postsynaptic Dendritic Spines, Associated with Autism. M. A. Papon¹, S. Marouillat¹, C. Antar², E. Cottureau¹, P. Vourc'h², S. Alirol¹, C. Andres², H. van Bokhoven³, J. Chelly⁴, H. Van Esch⁵, H.

proteins (NLGN, NMDAR subunits) for linking PDZ-domain containing proteins.

Conclusions: We confirm the contribution of *PTCHD1* gene mutations in X-linked ID and autism, therefore suggesting that this gene would have a crucial role in cognition and communication processes during the development of the central nervous system. We also indicate for the first time that PTCHD1 protein is present in both postsynaptic inhibitory and excitatory sites.

Stakeholder Experience Program

121 Stakeholder Experience

121.001 A Family Affair: Identifying and Examining Risk Factors for the Emotional and Behavioral Adjustment in Siblings of Children with Autism. K. L. Campe^{*1}, K. Porche², A. V. Snow³ and E. Hanson⁴, (1)*Boston Children's Hospital*, (2)*Boston Children's Hospital*, (3)*Boston Children's Hospital, Harvard Medical School*, (4)*Children's Hospital Boston*

Background: Sibling relationships are known to have a significant impact on the process of social and emotional development (Dunn, 1988). A number of studies have focused on the sibling relationship and the potential challenges faced by typically developing (TD) siblings of children who have an autism spectrum disorder (ASD) (Gold, 1993; Knott, Lewis & Williams, 1995; Hastings, 2003; 2007; Orsmond & Seltzer, 2007, 2009; Benderix & Sivberg, 2007; Petalas & Hastings, 2009). This study sought to examine how family demographic variables as well as behavioral characteristics of children with ASD impact the adjustment of their TD siblings.

Objectives: To identify and examine potential demographic and behavioral risk factors for the social, emotional and behavioral adjustment of TD siblings of children with ASD.

Methods: A sample of 2109 sibling pairs was drawn from the Simons Simplex Collection and the Boston Autism Consortium for use in the current project. Age ranges included children with ASD and their TD siblings between the ages of 4 to 18. To verify ASD diagnosis, the Autism Diagnostic Observation Schedule (ADOS) and Autism Diagnostic Interview-Revised (ADI-R), were performed. To confirm neurotypical development in the unaffected child, parents were asked to provide medical and educational information. Parents completed measures to

characterize the emotional and behavioral development of both children, including the Child Behavior Checklist (CBCL), and the Vineland Adaptive Behavioral Scales-II (VABS-II). In addition, parents provided demographic and familiar relations information. Preliminary analyses focused on testing the following demographic and behavioral risk factors: age and gender of sibling with ASD, NVIQ of child with ASD, and parent marital status. MANOVAs were performed to examine the impact of these variables on the TD sibling's CBCL and VABS-II scores.

Results: Analyses focused on the age of the child with ASD indicated that being younger than a sibling with ASD results in significantly higher scores on the following CBCL scales: rule-breaking, aggressive, externalizing problems, total problems, oppositional defiant problems, and conduct problems. Having a male sibling with autism resulted in significantly lower scores for the TD sibling on VABS communication and composite domains, as well as significantly higher scores on the attention subscale of the CBCL. Also, having a lower functioning sibling (in terms of NVIQ) resulted in significantly higher scores for TD siblings on the following CBCL subscales: somatic complaints, rule-breaking, aggressive, internalizing problems, externalizing problems, total problems, somatic problems, oppositional defiant problems, and conduct problems. TD children of divorced parents had significant scores on the somatic complaints, rule-breaking and conduct problems subscales.

Conclusions: Children who have a sibling with ASD who is male, older, and functioning at a lower level have a higher prevalence of social, emotional, and behavioral difficulties, particularly externalizing behaviors such as aggression, defiance, and attention problems. Future analyses will aim to further clarify the relationship between characteristics of children affected with ASD, family dynamics, and other demographic variables on the development of TD siblings.

121.002 College Students' Attitudes Toward Peers with High Functioning Autism. N. L. Matthews^{*1}, A. R. Ly² and W. A. Goldberg¹, (1)*University of California, Irvine*, (2)*University of Delaware*

Background: The transition to college for emerging adults with milder forms of autism

(HFA; Asperger's and high functioning autism) has become an increasingly salient concern for parents and professionals, yet it remains understudied. Reactions of typically developing college students to the presence of peers on the spectrum is of importance given the link between feelings of social belonging and retention of college students with disabilities (Belch, 2005).

Objectives: To compare university students' affective, cognitive, and behavioral attitudes toward vignette characters demonstrating social behaviors characteristic of HFA.

Methods: Participants were 195 college students at a four-year university in the southwestern U.S., aged 18-24 years ($M_{\text{age}} = 19.6$, $SD = 1.42$; 52% male). The majority of participants were Asian American (58.5%; 19.4% European American, 18% Hispanic or Latino, 3.2% Pacific Islander, and 1% African American). Participants read three vignettes depicting social interactions between peers in a university setting. The main character in each vignette was male and exhibited social behaviors characteristic of HFA. Students were randomly assigned one of three labeling conditions for the main character; HFA label, typical college student label, or no label. Participants completed an adapted version of the Multidimensional Attitudes Scale toward Persons with Disabilities (MAS; 33 items; Findler, Vilchinsky, & Werner, 2007) for each vignette main character and the 41-item Autism Knowledge questionnaire (Kuhn & Carter, 2006). Scores on the affect ($\alpha = 0.84$), cognition ($\alpha = 0.92$), and behavior ($\alpha = 0.86$) subscales of the MAS were averaged across the three main characters for each participant. Separate OLS regressions controlling for age, gender, and autism knowledge compared the three labeling condition groups on affect, cognition, and behavior subscale scores.

Results: No significant difference was observed on the affect subscale between students in the three groups. In contrast, for both the cognition and behavior subscales, students in the HFA label group reported significantly more positive attitudes than the group that received no label [cognition: $\beta = -0.30$, $t(189) = -3.80$, $p < .001$; behavior $\beta = -0.19$, $t(187) = -2.35$, $p = 0.02$]. However, the HFA and typical college student label groups did not differ significantly.

Conclusions: Results reveal a more positive disposition on the part of contemporary college students toward peers who display symptoms of HFA when they know that the person has HFA compared to not having the person labeled.

These experimental findings could mitigate parental and professional concerns about what would happen to HFA emerging adults in a typical university setting if the diagnostic label became known. Recent media and scientific awareness about the autism spectrum may have worked to create an accepting attitude on the part of the generation coming to adulthood. Additionally, increased community awareness may yield an effect similar to that of the diagnostic label condition in this study.

121.003 Medical Record Validation of Maternal Report of Prenatal Medical Conditions and Obstetric Interventions. P. Krakowiak^{*1}, C. K. Walker¹ and I. Hertz-Picciotto², (1)University of California, (2)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 accuracy of maternal report of prenatal conditions (pre-pregnancy obesity, diabetes and hypertensive disorders) and obstetric interventions (induction of labor and mode of delivery) reported in a structured telephone interview with medical records in a population of women of 2 to 5 year old children with and without a neurodevelopmental disorder.

Methods: A subset of participants from the CHARGE (CHildhood Autism Risks from Genetics and the Environment) Study with a confirmed diagnosis of ASD, developmental delays (DD) without ASD, or typical development (TD) and with both prenatal/delivery medical records and telephone interviews was included in the validation study. Kappa statistics measured agreement between self-report and medical records, while sensitivity and specificity indicated the validity of self-reported data. Bland-Altman plots depicted deviations in self-reported pre-pregnancy weight and body mass index compared with medical records.

Results: In general, mothers of affected children reported pregnancy and perinatal complications more accurately than control mothers. For diabetes, sensitivity ranged from 75% to 88% across diagnostic groups; specificity was 98% in all groups. Kappas ranged from 0.75 in controls to 0.92 in the DD group. Only 4% incorrectly reported whether or not they had preeclampsia, yielding a sensitivity of 65%, a specificity of 98% and a kappa of 0.66. For hypertension, sensitivity ranged from 33% in controls to 100% in the DD group; kappas ranged from 0.21 in controls to 0.42 in DD cases. Measurement error was small for weight and BMI and did not appear to vary by case status. Misclassification was differential by group when women were classified into obese and non-obese categories. Sensitivity ranged from 59% in controls to 86% in the DD group; kappas ranged from 0.68 in controls to 0.86 in DD cases. Low education and multiparity were associated with greater misclassification of hypertension; education level also influenced diabetes reporting. Self-reported diabetes and measurements to derive BMI appeared to have good validity. Misclassification increased when participants were classified into broad BMI categories. Self-reported hypertension had low validity and agreement, but this condition was also rare in this population. Mothers correctly distinguished vaginal deliveries from cesarean deliveries 100% of the time. Self-report of types of vaginal deliveries were less reliable, with 93% of women incorrectly reporting an operative vaginal delivery as a normal spontaneous delivery.

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. Maternal recall of the medical diagnoses and procedures included in this study was excellent, but varied by the condition under study, the health of the child, and maternal characteristics including education level and parity. This potential for exposure misclassification must be taken into consideration when designing and evaluating studies using self-report of pregnancy events.

121.005 Impact of a Support Group for Siblings of Children with ASD On the Quality of Sibling Relationships. J. Wolf*¹, M. Coffman¹, J. Bradshaw² and L. Herlihy³, (1)*Yale Child Study*

Center, (2)University of California, Santa Barbara, (3)University of Connecticut

Background: Research suggests that the quality of the sibling relationship is impacted, both positively and negatively, when one sibling has an ASD. Some positive characteristics include increased admiration for the affected sibling (Kaminsky and Dewey, 2001), and a greater amount of nurturing behaviors from the unaffected sibling (Abramovitch et al, 1987). At the same time, the sibling relationship may be characterized by less closeness, intimacy, reciprocity, interactive play, and in some cases increased physical aggression (Kaminsky and Dewey, 2001; Orsmond & Seltzer, 2007; Rivers & Stoneman, 2003). These aspects of the sibling relationship are consistent with the behaviors and social impairments characteristic of ASD, and may create a source of stress for unaffected siblings. The sibling relationship is typically the human relationship with the greatest longevity, and unaffected siblings often become caregivers for their sibling with ASD when parents are no longer able to provide care. Thus, it is in the interest of children with ASD as well as their unaffected siblings to ensure that unaffected siblings' needs are met, and to promote positive sibling relationship quality.

Objectives: To evaluate the effectiveness of a sibling support group in improving the quality of sibling relationships.

Methods: Five 10-week support groups for unaffected siblings of children with ASD were conducted across three age groups (two for ages 6-9, two for ages 10-12, one for ages 13-17; total n=28). An additional group (ages 10-12; n=4) was conducted as a waitlist control group. Group sessions were based on the Sibshop model (Meyer & Vadasy, 1994), with additional activities aimed at educating participants about the nature of ASD and teaching strategies for coping with stress. Several questionnaires assessing the quality of the sibling relationship were administered pre- and post-group (or waitlist period): the Sibling Relationship Questionnaire, Parent- and Self-Report forms (Slomkowski et al., 2001); the Sibling Relationship Scale (modified from Riggio, 2000); and the Satisfaction with the Sibling Relationship Questionnaire (McHale & Gamble, 1989).

Results: Unaffected siblings reported a significant increase in overall satisfaction in their sibling relationship following participation in the support group ($p=.01$). Several additional findings trended toward significance. Parents noted decreased negative behaviors in their unaffected children directed toward their affected siblings. Interestingly, across two measures, unaffected siblings reported a decrease in positive behaviors directed toward their affected siblings (such as time spent helping, playing, or talking together). No changes were found in the waitlist control group.

Conclusions: The sibling support group was effective in improving participants' overall satisfaction in their relationship with their sibling with ASD. The contrast between parent ratings and unaffected siblings' self-report ratings may suggest a general "diffusing" of intensity of the sibling relationship, which unaffected siblings perceive as less positive engagement and parents perceive as reduced negative behaviors. Alternatively, unaffected siblings may develop new insight or greater sensitivity through participation in the group that causes them to evaluate their own actions toward their siblings less positively.

121.006 When Are Adolescents with Autism Spectrum Disorder Better At Emotion Recognition Than Their Peers?. M. Brosnan*, E. Chapman, H. Johnson, B. Grawemeyer and L. Benton, *University of Bath*

Background: There is mixed evidence as to whether there is a deficit in recognising emotional expressions in Autism Spectrum Disorder (ASD). Variation occurs not only in the findings from different research groups but across different types of experimental stimuli. Emotion recognition in ASD has been investigated across different media - still photographs, moving video footage and voice recordings. There is also evidence to suggest that when there is a deficit in recognising emotion in human faces by people with ASD, this deficit does not extend to recognising emotion in cartoon representations of emotion. In this study we compare emotion recognition in ASD in all three types of emotion expression media (photo, video, voice) across both human stimuli (such as a photo of a human face) and animated stimuli (such as a cartoon face).

Objectives: To identify emotion recognition performance in ASD upon photo, video, and voice stimuli across both human and animated representations.

Methods: Participants were 37 adolescents (age 11-14) with a diagnosis of ASD (33 male, 4 female). 42 males and 39 females served as typically developing, age-matched controls. The first factor, 'Representation', had two levels: human and animated. The second factor was Media: photograph, video and voice. There were therefore six categories of stimuli (2 Representations x 3 Media), each of which contained six stimuli, totalling 36 stimuli. All participants were exposed via a computer display to all stimuli (in a randomised order) and had to identify the emotion being expressed in the stimuli. First we examined in Representation impacted upon emotion recognition, then the effect of each Media in isolation.

Results: For all analyses there were no significant differences between male and female control groups. For the Representation factor, there were no significant differences between ASD and control groups for the animated stimuli. For the human stimuli, however, the control groups, but not the ASD group, demonstrated significantly enhanced emotion recognition when compared to the animated stimuli. For the photo media in isolation, there was a significant interaction: Controls significantly outperformed the ASD group on human faces and the ASD group significantly outperformed controls on the animated faces. For the video media in isolation, controls were significantly more accurate than the ASD group for both types of representation. For the voice media in isolation, there were no group differences in recognising animated sounds, but controls had significantly enhanced recognition of emotion in human voice, whereas the ASD group did not.

Conclusions: For photographic and voice media, the emotion recognition deficit in ASD was only evidenced for human, not animated, stimuli. The ASD group did not demonstrate an advantage for recognising emotions within human faces and voices, whereas the control groups did. The ASD demonstrated an advantage over controls for recognising emotion in animated (cartoon) still images. This advantage did not extend to video

media and may reflect different strategies being employed to recognise human and animated representations of emotion.

121.007 Background and Clinical Characteristics of Young Adult Males with Autism Spectrum Disorders Sentenced to Prison for Violent or Sexual Offences. B. Hofvander*¹, E. Billstedt², M. Wallinius³ and H. Anckarsäter², (1)*Department of Clinical Sciences, Malmoe, Lund University*, (2)*University of Gothenburg*, (3)*University of Lund*

Background: Among young people, violent crime is a leading cause of reduced health, disability, and death world-wide and offenders as a group are at particular high risk of becoming victims of violence themselves. Violent crimes are perpetrated by a small group of individuals in society and an even smaller group is responsible for a disproportionate number of these crimes. The majority of this small group of repetitive offenders has had childhood adjustment problems, early onset of crimes and substance abuse. The prevalence and significance of socio-communicative deficits in violent criminals is still largely unknown. For the detection, treatment and prevention of further violent criminality of convicts with autism spectrum disorders (ASDs) it is important to describe the clinical and criminological characteristics of these offenders and follow them after discharge.

Objectives:

Early onset behaviour disorders (i.e. oppositional defiant disorder, conduct disorder, attention deficit-/hyperactivity disorder and ASDs) form the antecedents of complex psychiatric problems with an increased risk for psychosocial marginalization and recidivistic criminal careers in adulthood. The current study investigates the clinical, psychosocial and criminological characteristics in a subgroup of young adult criminal offenders with ASDs, the coexistence of ASD and other early onset behaviour disorders as well as personality disorders.

Methods:

Young adult male offenders (18-25 years of age) sentenced for "hands-on" violent and/or sexual offences who were serving prison time in correctional facilities (n=9) in the Western Region of the Swedish Prison and Probation Service were

invited to participate in the study. The project started in April 2010 and closed in July 2012 when 271 subjects had taken part in the study. The participation rate was about 70 %. Clinical diagnostic assessments (SCID-I and -II), psychosocial history (including antisocial behaviours/ substance abuse), basic neurological examination, structured neuropsychiatric status, neuropsychological testing, and genetic work-up were carried out. In addition to a structured DSM-IV based interview on ASD criteria, the Asperger's syndrome /high functioning autism Diagnostic Interview (ASDI) was used. When possible, collateral DISCO interviews or ADOS ratings were made.

Results: This group of young males with ASD and antisocial behavior has a complex picture of coexisting mental health problems. Patterns of psychiatric comorbidity (including substance use disorders), neuropsychological data, characteristics of their background, index crime and crime history will be reported.

Conclusions:

The study emphasizes the importance of a broad focus when assessing for psychiatric comorbidity in individuals with the combination of antisocial behaviour and ASD. Data on clinical, psychosocial and crime characteristics will possibly increase our knowledge of which ASD individuals are at highest risk of an antisocial development and which kinds of crimes individuals with ASDs are most likely to commit.

121.008 Child, Parental, and Contextual Factors That Predict Parenting Stress in Families of Young Children with ASD Over a 2-Year Period After Diagnosis. A. Zaidman-Zait*¹, P. Miranda¹, P. Szatmari², S. E. Bryson³, E. Fombonne⁴, I. M. Smith⁵, W. Roberts⁶, T. Vaillancourt⁷, J. Volden⁸, C. Waddell⁹, L. Zwaigenbaum⁸, S. Georgiades², E. Duku² and A. Thompson², (1)*University of British Columbia*, (2)*Offord Centre for Child Studies & McMaster University*, (3)*Dalhousie University/TWK Health Centre*, (4)*Montreal Children's Hospital*, (5)*Dalhousie/TWK Health Centre*, (6)*University of Toronto*, (7)*University of Ottawa*, (8)*University of Alberta*, (9)*Simon Fraser University*

Background:

Higher levels of parenting stress have been found in parents of young children with autism spectrum disorder (ASD) compared to those with other

disabilities (Estes et al., 2009). Previous studies have identified numerous child variables that are related to increased parenting stress; however, parental and contextual predictors have been examined less extensively. In addition, most studies of parenting stress have included small sample sizes and have utilized data collected at only one time point.

Objectives:

The purpose of this study was to examine how parental and contextual variables predict parenting stress after controlling for the effects of child factors that have a known impact. Specifically, after controlling for children's autism severity, daily living skills, and behavior problems, we investigated whether parental education, socio-economic status (SES), parent coping skills, family functioning, and social support predicted parenting stress over a 2-year period immediately following diagnosis, in a systematic sample of young children with ASD.

Methods:

Data were drawn from the Canadian Pathways in ASD study and included 205 children and their parents. Data were collected within 4 months of diagnosis (T1; mean child age = 39.4 months) and 24 months later (T2). Parents completed a family demographic survey; the Parenting Stress Index-Short Form (PSI-SF); the Ways of Coping Scales (WCS); a Family Relationships Questionnaire; a Social Support Survey; the Vineland Adaptive Behavior Scales, 2nded. (VABS-II); and the Child Behavior Checklist 1.5-5 (CBCL). In addition, the Autism Diagnostic Observation Schedule (Lord et al., 2000) was administered and the autism severity score (Gotham, Pickles, & Lord, 2009) was used as one of the child variables. Hierarchical multiple regression analyses were conducted.

Results:

In the regression analysis, three child-level variables (i.e., autism severity on the ADOS, behavior problems on the CBCL, and daily living skills on the VAB-II) were entered in the first block, and accounted for 16% of the variance in parental stress at T1 ($F=13.03, p<.001$). Next,

SES and parental education were entered, with no significant effect. Parent coping strategies from the WCS were entered in the next step and accounted for an additional 16.6 % of the variance (confrontive coping, $\beta=.18, p=.004$ and positive reappraisal, $\beta= -.18, p=.009$). Finally, social support and family functioning were entered together and accounted for an additional 23.3% of the variance at T1. At T2, parental coping strategies (escape avoidance, $\beta=.21, p=.004$) and social support and family functioning accounted for an additional 7% and 5% of the variance, respectively, over and above the predictors at T1. The overall model explained 68% of the variance in parental stress at T2 ($F =15.1, p<.001$).

Conclusions:

While numerous child variables impact parenting stress, parents' coping skills and the social supports available to them both within and outside of their families also significantly affect their experiences of stress over time. Programs that aim to deliver family-centred services should endeavor to provide social supports and promote adaptive coping strategies in parents of children with ASD, in addition to providing early intervention.

Neurophysiology Program

122 Neurophysiology : (1) Perception and (2) Measurements of Treatment

122.001 Gamma Oscillations Associated with the Perception of Simultaneity in Autism Spectrum Disorder. D. A. Menassa^{*1}, C. Falter² and S. Braeutigam¹. (1)*Oxford Human Brain Activity Centre*, (2)*University of Groningen*

Background: Temporal event coding is the perception of visual stimuli as simultaneous or asynchronous and ASD individuals excel in psychophysical tests of temporal event structure. Gamma oscillations are thought to mark neuronal synchrony in cognitively active states and have been consistently reported to show a burst in activity in visual events relating to the perception of coherent objects. Thus, oscillatory brain activity in the gamma range (>30Hz) has been hypothesized to facilitate coherent action of neuronal processes participating in the same cognitive processes. Although gamma oscillation power differences have been reported in ASD individuals, results vary depending on the visual paradigm that has been used.

T. Wang^{*1}, L. Soorya², D. B. Halpern¹, S. Soffes¹, M. Gorenstein¹ and J. D. Buxbaum¹, (1)Mount Sinai School of Medicine, (2)Rush University

Objectives: The aim of this study was to test oscillatory synchrony in the gamma range in a visual simultaneity task in a group of high-functioning ASD patients versus age-matched and IQ-matched typically developing subjects (TD).

Methods: 17 ASD (mean age = 24; ADI-R and ADOS-confirmed) and 17 TDC (mean age = 26) were recruited with appropriate ethical approval. Individuals participated in a visual simultaneity task in the magnetoencephalography (MEG) scanner at the Oxford Human Brain Activity centre at the University of Oxford and were presented with three conditions on a screen: a simultaneous condition (two vertical bars appearing on a screen at the same time); a short condition (17 ms delay of appearance for the second bar); and a long condition (117 ms delay; not reported here). Participants judged the stimuli as simultaneous or asynchronous with a response cue of 1500 ms and completed 4 experimental blocks consisting of 60 trials each. Time-frequency analyses were performed on individual epochs.

Results: Our behavioural data show that ASD individuals significantly discriminate between the short and simultaneous conditions ($p < 0.05$) compared to TD subjects, who perceive both conditions as being similar. Our time-frequency analyses show a burst of phase-locked gamma-band activity between 40 and 60Hz in the short condition during early visual processing between 50 and 80ms after stimulus onset in the TDCs. However, ASD individuals show no gamma-band activity for this condition ($p < 0.001$). This localises to the occipital pole. In the simultaneous condition, gamma-band activity was similar between both groups.

Conclusions: Discrimination of the timing of events in ASD individuals during early visual processes might suggest a cognitive strategy that does not involve oscillatory synchrony in the gamma range over the occipital pole. Although gamma-band bursts are thought to support visual binding processes, ASD individuals still have an enhanced access to early visual processing of perceptual simultaneity, which may not involve synchrony in the gamma range.

Background: Social skills groups are a common treatment for individuals with autism spectrum disorders (ASD). However, research evaluating the efficacy of such treatments is limited and more work is needed to identify effective techniques for improving social skills. Several neuroimaging studies have found that individuals with ASD underactivate key brain regions involved in social cognition. However, 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. This suggests that a cognitive behavioral approach to social skills treatment may help increase not only social behavior but also the activation of normative neural systems that support social functioning.

Objectives: This study aims to examine the neural and behavioral effects of two approaches to social skills groups: cognitive behavioral therapy (CBT) and child-directed play. Here we present the short-term neural effects using two previously validated fMRI tasks that probe targeted skill domains: 1) interpreting communicative intent, and 2) processing gaze direction in emotional faces.

Methods: Verbally fluent children with ASD, 8-11 years of age, were randomized to the CBT or child-directed play group. Both treatment approaches consisted of 12 weekly 90-minute sessions (4-6 children in each group) with a concurrent parent group. Behavioral assessments and fMRI were conducted at baseline, end of treatment, and at a 3-month follow up. While undergoing fMRI, children viewed cartoon drawings of characters in a conversational setting while listening to short scenarios ending with a comment made by one of the characters. Participants decided whether the speaker meant what she said.

Results: Following treatment, children in the CBT group showed greater activity in the ventromedial prefrontal cortex (vmPFC), the ventrolateral PFC, the inferior frontal gyrus, and the superior temporal gyrus (STG)/temporal pole relative to baseline. In contrast, children in the child-directed

play 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), emotion recognition (STG/temporal pole) and language processing (inferior frontal gyrus) compared to children in the play group.

Conclusions: Further analyses are being conducted, but these results suggest that a CBT approach that capitalizes on top-down explicit processing may facilitate increased activity in brain regions playing an important role in social cognition after a relatively brief intervention period. It will be important to assess whether these changes are maintained at follow up. By exploring the relationship between changes in brain activity and changes in social behavior, we hope to develop hypotheses about the neural mechanisms underlying response to treatment.

122.003 Neurophysiological Correlates of Tactile Sensitivities in ASD. S. Khan¹, M. Tommerdahl², M. G. Kitzbichler¹, S. Ganesan¹, N. R. Shetty¹, M. R. Herbert¹, M. S. Hämäläinen¹ and T. Kenet^{*1}, (1)*Massachusetts General Hospital*, (2)*University of North Carolina*

Background: Abnormal sensory processing in general, and in the tactile domain in particular, is widespread in autism spectrum disorders (ASD), but no physiological basis for those aberrant sensitivities has ever been elucidated. Establishing the physiological correlates of these tactile abnormalities is necessary not only to further enhance our understanding of the biological basis of ASD, but also to inform possible treatments and therapies.

Objectives: Given prior studies showing abnormal behavioral patterns following tactile fingertip vibrations in ASD (Tommerdahl et al., 2007 & 2008), we chose to investigate the neural correlates of the cortical response to such vibrations.

Methods: We used magnetoencephalography (MEG), to record cortical responses to 500ms of 25Hz pneumatic vibrations using latex tactors on the fingertips of 32 participants ages 8 to 17, of which 15 were diagnosed with ASD. We then mapped the responses from the MEG sensors onto cortical space, and focused on the

neurophysiological responses in the primary somatosensory cortex (S1). We also recorded peripheral responses on the median nerve in a parallel group of participants.

Results: All participants, regardless of diagnosis, showed a clear sustained 25Hz cortical response to the tactile vibrations. In the control group, we also found a component of the response consisted of cortically generated harmonics at 50Hz, indicating a non-linear neuronal response pattern in the cortex. Such harmonics were absent in our peripheral recordings, confirming they are generated cortically. This non-linear component of the response to vibrations was largely reduced in the ASD group, indicating a more veridical, linear, response to tactile vibrations in that group. The degree to which the 50Hz harmonics component was present in the cortex in any one individual correlated with the severity of ASD as measured using the ADOS score. Furthermore, the magnitude of the harmonics component in each participated was also significantly correlated with the individual scores on the tactile component of the sensory profile questionnaire, indicating that the degree of linearity in the cortical neural response of ASD individuals in S1 was predictive of the magnitude of aberrant tactile sensitivities in each individual.

Conclusions: We mapped neurophysiological correlates of abnormal tactile sensitivities often associated with ASD. These neurophysiological correlates indicate that an abnormally linearized cortical neuronal response, probably due to reduced local inhibitory interactions, is directly correlated with behavioral tactile abnormalities in ASD as measured using a behavioral questionnaire.

122.004 Neurophysiological Measures of Sensory Processing and Integration Are Predictive of Autistic Symptom Severity, but Not of Sensory Sensitivities, in a Group of High-Functioning Children and Adolescents with ASD. A. B. Brandwein*, J. J. Foxe, T. S. Altschuler, J. S. Butler, J. C. Bates and S. Mölholm, *The Sheryl and Daniel R. Tishman Cognitive Neurophysiology Laboratory, Albert Einstein College of Medicine*

Background: Difficulties processing and integrating sensory information have long been noted in individuals with autism spectrum disorders (ASD), and it has been suggested that this contributes significantly to some of the major

symptoms of autism, including aberrant language development, unusual and repetitive behaviors, and deficits in social perception. In light of these potentially far-reaching consequences, surprisingly few studies have explored the neurophysiological basis of sensory processing atypicalities, or how these might relate to the clinical presentation of ASD.

Objectives: To assess whether neurophysiological measures of sensory processing and multisensory integration are predictive of autistic symptom severity and of sensory sensitivities in high-functioning children and adolescents with ASD.

Methods: The sample consisted of 44 individuals between the ages of 6-17 years who met criteria for a diagnosis of ASD. Event related potentials (ERP) data were collected while participants performed a simple speeded detection task in response to auditory and visual stimuli presented together and alone, in random order. The ERP components of interest were the major sensory deflections recorded in the first 200 ms, decided a priori and including the auditory P1, N1a, N1b, and N1c, the visual P1 and N1, and 3 multisensory effects between 100-210 (based on prior research). A linear regression analysis was conducted to investigate whether ERP responses to basic auditory, visual, and audiovisual stimuli predict the severity of current ASD symptoms, as indexed by the Calibrated Severity Scores (CSS) from the Autism Diagnostic Observation Schedule (ADOS). An additional hierarchical linear regression analysis examined whether these same ERP measures predict the severity of visual and auditory sensitivities (VAS), as reported by parents on the Short Sensory Profile. Both analyses controlled for participant characteristics (age, sex, VIQ, PIQ, race, and maternal education) that were shown to correlate with our outcome measures.

Results: The linear combination of ERP measures was significantly related to CSS, with about half of the variance of autistic symptom severity in the sample accounted for by measures of basic sensory responses and multisensory integration. The best ERP predictors of CSS were the auditory N1a and N1b, and multisensory integration between 100-130 ms over frontal sites. In contrast, the linear combination of ERP measures did not account for a significant proportion of the

variance in VAS after controlling for the effects of verbal IQ (which was highly correlated with VAS).

Conclusions: Brain responses to basic sensory stimuli predict severity of autistic symptoms in a group of high-functioning individuals with ASD. This provides preliminary evidence that early sensory processing differences may well contribute to the core symptoms of ASD. Perhaps even more importantly, this study supports the use of ERPs as a potential tool for developing endophenotypic markers for ASD, an approach that may be crucial in the future for identifying, characterizing and subtyping this complex group of neurodevelopmental disorders.

122.005 Comparison and Recommendations for Processing EEG Data in Children with Autism and Typical Developing Controls. K. McEvoy* and S. S. Jeste, *UCLA*

Background: A particularly useful and increasingly utilized tool for studying children with ASD is quantitative electroencephalography, qEEG, which allows for analysis of the power at different established frequency bands. qEEG, as a biomarker, has the potential to define subgroups of children with ASD, which can then inform targeted treatment. However, different procedures for processing qEEG data can have a major impact on final power measurements, which leads to difficulties in replicating findings. In order to maximize the utility and reliability of qEEG, a comparison of different processing methods is needed.

Objectives: We have investigated the stability and reliability of qEEG in typically developing (TD) children, the way in which different decisions in the data processing stream affect the data, and whether these parameters differ between children with ASD and TD controls. This project addresses many methodological questions and compares decisions at various processing steps. Some of the main questions we seek to answer include: 1) What is the minimum amount of clean EEG data required to produce a stable measurement of the power in well-known frequency bands (theta, alpha, beta, and gamma); 2) How stable are the measurements of these frequencies across the course of the single recording session (~5 minutes), across multiple time points (~3 months), and at different ages (2.5 – 6 years old); 3) How does the selection of the EEG reference and electrode groupings affect the

measurements of these frequency bands; and (4) How do the answers to these questions differ between children with ASD and age-matched TD controls.

Methods: EEG was recorded while children were at rest with their eyes open, watching a video of bubbles. A minimum of 2 minutes of data were obtained from both children with ASD and TD controls. EEG data were bandpass filtered from 1 to 50 Hz, divided into one second segments, and examined for artifact contaminated data. Various crucial decision points in a typical qEEG processing stream were altered and compared for their impact on standard statistical measurements of frequency power. After measureable changes in the EEG data processing stream were made, the data were transformed into the frequency domain using a Fast Fourier Transform (FFT) in order to obtain a measurement of the Power Spectral Density (PSD) at standard frequency bands.

Results: Given the large number of experimental manipulations and comparisons, all results are too numerous to summarize. However, a few brief, but important findings include the following. 1) The number of segments used to calculate frequency power differs across frequency bands. 2) Different artifacts can have very different effects on each frequency band. 3) Selection of electrode groupings must be performed with great care.

Conclusions: The decisions that a researcher makes on how to process and clean their qEEG data greatly affects the results. If qEEG is to become a useful biomarker across labs, then standardized procedures should be followed. Based on our many comparisons, we provide recommendations for others who use high-density electrode systems to measure neural activity in children with ASD and TD children.

122.006 Neural Plasticity and Intervention: Effects of the PEERS Program On EEG Activity and Respiratory Sinus Arrhythmia. S. Stevens*, A. V. Van Hecke, J. Wasisco, A. M. Carson, J. S. Karst, K. A. Schohl, B. Dolan, R. J. Rimmel, N. Fritz, G. McDonald, A. Reveles and J. Kahne, *Marquette University*

Background: Few studies have examined neurophysiological plasticity due to intervention in autism spectrum disorders (ASD) despite the significant neural discrepancies identified in this population (Minshew, 2007). Here, we examine

change in EEG power levels in the beta and gamma bands in those cortical areas of the brain associated with social behavior (Adolphs, 1999) in response to PEERS, a social skills intervention (Laugeson et al., 2009). Further, autonomic regulation via the vagus nerve, measured as Respiratory Sinus Arrhythmia (RSA), may serve as a biomarker of social behavior (Porges, 2001). RSA is therefore also assessed as a potential subcortical outcome measure. This study aims to explore the neurophysiological alterations associated with completion of an empirically supported behavioral treatment for ASD.

Objectives: Investigate changes in EEG beta and gamma activity and RSA as they relate to completion of a social skills intervention program in adolescents with ASD.

Methods: Forty adolescents (11-16 years old) were randomly assigned to an Experimental Group (EXP) or Waitlist Control Group (WL). Heart rate and neural activity, as measured by continuous EEG, were assessed pre- and post-intervention/delay during a 3-minute resting, eyes open condition. Average beta (13-30 Hz) and gamma (30-45Hz) band activity from left and right hemisphere electrodes was then calculated and compared across time (pre-/post-treatment) and group assignment (EXP/WL). Average beta band power was analyzed in the frontal, parietal, and temporal lobes. Average gamma power and coherence were analyzed in the frontal, frontal midline, parietal midline, and parietal-temporal regions. Beta and gamma findings were initially submitted as distinct projects but combined on request, explaining differences in data analysis choices. Final analyses would, however, be performed in a consistent manner.

Results: Preliminary results indicate a group x time x location interaction for gamma power, $F(5, 27) = 2.45$, $p < .05$, partial $\eta^2 = .31$. Examination of data reveals midline frontal and parietal, and left parietal-temporal gamma power increases in the EXP group but not in the WL group. Gamma coherence measurements indicated an increase in left-right frontal coherence in the EXP group, $t(16) = 2.33$, $p < .05$. Beta power analysis reveals a time x group interaction in the left frontal lobe, $F(1, 30) = 4.85$, $p < .05$, partial $\eta^2 = .14$, and left parietal lobe $F(1, 29) = 4.641$, $p < .05$, partial $\eta^2 = .14$, again

reflecting increases in the EXP group but not the WL group. No significant change in RSA was found.

Conclusions: Preliminary findings suggest that participation in the PEERS treatment program is associated with change in cortical brain regions but not in subcortical, cardiac regulatory systems. Beta band activity is associated with focused attention and brain activity synchronization, and gamma with higher-order information processing and neural synchronization, all of which are atypical in ASD (Dawson, 2008; Blinkowska, 2006; Minshew, 2007; Murias 2007). Further, atypical lateralization, specifically right asymmetry has been associated with increased symptom severity in the ASD population (Sutton et al., 2004). We suggest that the current results may be indicative of neural 'correction' in response to treatment.

122.007 Visual Fixation Preferences in Autism: A Randomized Controlled Trial of Intranasal Oxytocin. L. Strathearn*¹, D. A. Bastian², J. Jung¹, S. Kim¹, U. Iyengar¹, S. Martinez¹ and P. Fonagy³, (1)*Baylor College of Medicine*, (2)*Brigham Young University*, (3)*University College London*

Background: Autism spectrum disorder (ASD) is a complex neurodevelopmental disorder characterized by severe social/communication deficits, repetitive behaviors and fixated interests (proposed DSM-5 criteria). Recently, studies have shown that the neuropeptide oxytocin enhances social communication while reducing repetitive behaviors in some ASD patients (Andari et al. 2010; Guastella et al. 2010; Hollander et al. 2003). However, no prior study has examined the effect of oxytocin on fixated interests in children with ASD.

Objectives: The objective of this study was to examine the effect of intranasal oxytocin on fixated interests in children and adolescents with ASD. We hypothesized that ASD subjects would show a visual preference for more highly organized or structured ("systemized") real-life photographs, compared with matched control subjects, and that this preference would be reversed after administration of intranasal oxytocin.

Methods: As part of a randomized double blind placebo-controlled crossover study, 32 subjects (16 ASD and 16 matched control males; mean

age 13 years; range 8-19 years) were administered either intranasal oxytocin or placebo on their first study visit and the alternate solution on a subsequent visit two weeks later. Oxytocin administration was counterbalanced between subjects across study visits. On each occasion, participants then viewed 14 slides, each containing four related pictures that differed on the degree of systemization (i.e. different arrangements of people, animals, objects or scenes). Picture position on each slide was pseudo-randomized across study participants. Visual preference was determined using an automated eye tracker which calculated fixation times and counts within each of the four regions of interest. Mixed-effects linear regression models were used to determine the relationship between oxytocin administration and visual fixation preferences in ASD and control subjects, adjusting for visit order and picture position.

Results: Significant 3-way interactions were found for both fixation time and count; oxytocin significantly reduced the tendency for ASD subjects to view more highly systemized pictures compared to receiving placebo, whereas the opposite pattern was seen for control subjects. Oxytocin significantly reversed the preference of ASD subjects to view more highly systemized pictures.

Conclusions: This study provides additional evidence for the potential benefits of oxytocin in ASD to diminish fixated interests, in addition to reducing repetitive behaviors and enhancing social communication.

122.008 Individual Differences in Affective Social Perception in ASD: Neural, Behavioral, and Psychiatric Contributions. J. C. McPartland*¹, A. Naples¹, M. Coffman¹, A. Kresse², C. E. Mukerji¹ and R. Bernier², (1)*Yale Child Study Center*, (2)*University of Washington*

Background: The social motivation hypothesis posits that reduced social drive leads to inattention to people and consequent failure of developmental specialization in experience-driven brain systems for social perception. Abnormalities in face perception and in the action perception system are documented throughout the lifespan in ASD, but heterogeneity is poorly understood. The current work explores the influence of individual differences in neurocognitive characteristics and

psychiatric symptomatology on social brain circuitry underlying emotion perception.

Objectives: To apply an innovative experimental paradigm to (a) examine electrophysiological markers of both emotional face processing and action perception and to (b) explore relationships among event-related potential (ERP) markers of social perception and neurocognitive and psychiatric characteristics.

Methods: The paradigm employed a novel stimulus set of 210 unique 3D photorealistic face stimuli capable of producing movements consistent with human musculoskeletal structure. Children with ASD (N=27) and matched controls (N=35) viewed a 500ms static initial pose, which segued into 500ms facial movement of three types: (1) affective movement (fearful expression); (2) neutral movement (puffed cheeks); and (3) biologically impossible movement (upward dislocation of eyes and mouth). ERPs (reflecting stages of face processing) were time-locked to onset of static face stimuli, and oscillatory EEG power in the mu range (reflecting activation in the action-perception system) was extracted during periods of facial movement. Comorbid symptoms were measured with the Child Behavior Checklist (CBCL).

Results: An ERP index of face identification (N170) differentiated clinical groups, such that individuals with ASDs exhibited delayed N170s to faces [$F(1,60) = 18.3, p < .001$]. A main effect of emotion on N170 latency [$F(3,60) = 4.419, p = .005$] revealed that neutral faces elicited faster N170s than expressive facial. Bayesian structural equation models were applied to examine shared versus distinct latent sources of variability for ERPs and EEGs to faces, as well as an integrative model incorporating brain activity and behavior. These models revealed that early markers of face processing (P1) predicted later markers (N170; $p = .023$). However, in models incorporating diagnostic category and reported social problems from the CBCL, this relationship was attenuated; both social problems and diagnosis predicted N170 latency ($ps = .082$ and $.004$, respectively), and social problems uniquely predicted variability in the P1 ($p = .034$). Bivariate models investigating these effects revealed that, across groups, N170 latency was significantly associated

with comorbid symptoms: social difficulties ($r = .439, p = .001$), aggression ($r = .306, p = .019$), externalizing behavior ($r = .339, p = .009$), affective problems ($r = .363, p = .005$), inattention and hyperactivity ($r = .414, p = .001$), cognitive problems ($r = .465, p < .001$), and obsessive-compulsive behaviors ($r = .386, p = .003$).

Conclusions: Neural responses differentiated diagnostic groups and explained transdiagnostic variability in comorbid symptoms. Results suggest observed heterogeneity in ERP indices of social perception may reflect individual differences in neurocognitive and psychiatric factors. These findings have significant implications for individualized treatment.

Neurophysiology Program

123 Neurophysiology 1

123.001 1 Adolescents with ASD Show Attenuated Neural Response to Reciprocal Eye Contact. A. Naples*, M. Coffman, C. E. Mukerji, R. Tillman and J. C. McPartland, *Yale Child Study Center*

Background:

Problems with eye contact represent one of the most pervasive and early manifesting symptoms of autism spectrum disorders (ASDs). Prior electrophysiological research in gaze perception in ASD has focused primarily on passive observation of social information, failing to address the interactive nature of eye contact. Our preliminary work in typical development (TD) revealed two event-related potential (ERP) indices of detection of shared gaze in real time during reciprocal interactions: the N170, measured at occipitotemporal electrodes, and the P300, measured at central electrodes. The temporal dynamics of brain activity during reciprocal social interactions in ASD remain largely unexplored.

Objectives:

By applying experimental paradigms in which on-screen faces responded to participant gaze, this study investigated brain activity evoked by reciprocal eye contact. Our objective was to evaluate the characteristics of ERP markers of shared gaze in individuals with ASD and to explore their relationship to social behavior. We

predicted that individuals with ASD would not differentiate changes in responsive gaze at early or late ERP components and that the N170 would be less sensitive to point of gaze in individuals with ASD versus TD.

Methods:

ERPs were recorded from 20 high-functioning adolescents with ASD and 20 matched TD controls using a 128 electrode Geodesic Hydrocel Net. Eye movements were recorded from high-speed remote eye-tracking system (SR-Research Eyelink 1000) integrated with a stimulus presentation computer and EEG recording. Through co-registered ET and EEG, the experimental paradigm was controlled by participant gaze. Trials began with a peripherally-presented fixation crosshair followed by a centrally-presented face displaying either direct or averted gaze. Contingent upon participant fixation, the face responded by either looking at the participant (eye contact) or looking away from the participant (averted gaze). ERPs were time-locked to face movement; the N170 was extracted from occipital electrodes and the P300 was extracted at central electrodes.

Results: Preliminary results show an enhanced P300 to eye contact in typically developing individuals that was attenuated in ASD (mean amplitude TD 1.7 μ V, mean amplitude ASD - .41 μ V). Among typically developing individuals 73% of fixations were to eye-regions of the face, and the N170 to responsive eye contact was attenuated on trials in which participants fixated to non-eye regions of the face (mean difference in amplitude = 1.94 μ V). Analyses in progress investigate the relationship between point of gaze and neural response to eye contact in individuals with ASD.

Conclusions:

We demonstrate an electrophysiological marker of shared gaze that is absent in individuals with ASD. We interpret this finding to indicate that individuals with ASD are less sensitive to socially-relevant changes in gaze even when these changes are contingent on their own behavior. That these individuals differentially respond to the outcomes of their own gaze shifts suggests a potentially different approach to learning about

their environment and others during development. By exploring brain response to shared gaze in a context driven by participant behavior we gain a more nuanced profile of social brain dysfunction and a potential mechanism for defining subgroups based on performance during interactive assessment.

123.002 2 Electroencephalographic (EEGs) Abnormalities in Individuals with Autism Spectrum Disorders (ASDs). D. M. Simula¹, M. Carta², D. Serra², F. Piras², R. Fadda^{*3}, P. Pusceddu², S. Sotgiu¹ and G. S. Doneddu², (1)University of Sassari, (2)Azienda Ospedaliera Brotzu, (3)University of Cagliari

Background: ASDs are neurodevelopmental disorders of unknown etiology characterized by social and communication deficits and the presence of restricted interests/repetitive behaviors. Recently, there has been an increasing interest in the occurrence of epileptiform electroencephalograms (EEGs) in ASDs even in the absence of epilepsy (Tuchman, 2011). Rates as high as 60% have been reported and some investigators proposed that these abnormalities may play a causal role in the autism phenotype (Spence & Schneider, 2009). However, there are not robust evidences concerning specific risk factors in children with ASDs, like for example symptoms severity, which might be used to predict which children will develop epilepsy and/or EEG abnormalities.

Objectives: This study examined the frequency and the nature of EEGs abnormalities in a sample of 57 individuals with ASDs, enrolled at the Center for Pervasive Developmental Disorders in Cagliari (Italy).

Methods: Our sample consisted of 49 males and 8 females, aged 1-17 years (average: 9,05 years), with a diagnosis of ASDs (70% with Autism, 25% with Pervasive Developmental Disorder-not otherwise specified, 5% with Asperger Syndrome). Participants were characterized by borderline intellectual functioning, as measured by different scales, like the Bayley Scales, the Leiter-R, the WPPSI-3 and the WISC-3. The heterogeneity of the measures employed to assess the intellectual functioning was due to the different developmental characteristics of the participants. Each participant was tested with an "awake-sleep" EEG registration, performed with the System 10-20 of Jasper, after sleep deprivation.

Results: The 58% of the participants showed EEGs abnormalities, in which the anomalies were both nonspecific changes, such as slowing or asymmetry, and epileptiform discharges, consisting of spikes or sharp waves discharges, sharp slow waves, generalized spike-wave, and generalized polyspikes are seen. The EEGs abnormalities were mainly localized in the temporo-occipital region, according with a previous study (Spence and Schneider, 2009) and, less often, in the frontal regions. These anomalies may occur in individuals without seizures, and their presence should not be considered as evidence of epilepsy: rather, these EEG changes are considered to be signs of cerebral dysfunction. The prevalence of epilepsy was the 7%.

Conclusions: The EEG findings in our sample confirm what was found in previous studies, about the rate of EEGs abnormalities in individuals with ASDs and their main localizations (Lee et al., 2011). Since in our sample the rate of EEGs anomalies is higher than the general population, these results suggests that an underlying pathophysiology in ASDs might increase the risk of epileptiform anomalies and epilepsy. It might be of interest to identify specific ASDs phenotype which might be at higher risk of EEGs abnormalities.

123.003 3 Gamma Synchronization During Face Processing Is Associated with Social Motivation. C. Cuevas*, A. Naples, C. H. Cheung, L. Mayes and J. C. McPartland, *Yale Child Study Center*

Background: ASD is characterized by deficits in social interaction and communication. EEG studies have demonstrated difficulties in face processing by individuals with ASD as evident by a delayed and diminished N170 response. This atypical N170 has been proposed as a secondary effect of a primary deficit in social motivation, which is considered a driving influence in the development of face expertise. Cheung et al. (2010) found that social personality traits (extraversion versus introversion) in typically-developing individuals modulated neural response to faces such that extraverts showed an enhanced face inversion effect. The present study further investigated the link between social motivation and face processing by examining gamma synchrony, which has been

proposed as an indicator of long-distance interactions among neural regions. An alternative interpretation of face processing anomalies in ASD is that cognitive factors, rather than social motivation, could account for atypical face processing. Two previous studies have shown increased gamma synchrony in response to faces in typically-developing adults. Klopp et al. (2000) showed increased coherence 160-230 ms post-stimulus onset between the fusiform gyrus and other brain regions, and Rodriguez et al. (1999) showed increased synchrony between parieto-occipital and frontotemporal regions 200-260 ms post-stimulus onset.

Objectives: The current study sought to contrast predictions of social versus cognitive influences on face perception. To study how social personality traits influence face-related activity, the relationship between gamma synchrony and social motivation was examined. The social motivation hypothesis would predict significant correlations between gamma synchrony and extraversion, while cognitive accounts would predict no relationship.

Methods: 96 typically-developing adults (34 male) were pre-screened with the Eysenck Personality Questionnaire Revised Short Scale (EPQ-R) for high or low (+/- 1 SD) scores on the extraversion subscale. 24 extreme scorers (14 extraverts, 10 introverts) viewed 60 trials each of upright and inverted faces, while EEG was recorded with a 128-channel Geodesic Sensor Net. EEG signals were decomposed to the gamma frequency band (30-50 Hz) using wavelet analysis based on 4-6 cycles, a 148 ms window size and 547.2 ms epochs, including a -25.6 ms baseline. Synchrony based on phase difference was calculated between all channel pairs and measured between 0 and 1, where 1 indicates two perfectly synchronized signals.

Results: ERP results indicated that the inversion effect significantly interacted with personality type: $F(1, 22) = 5.11$, $p = .03$, $MSE = 0.86$, $\eta^2_{\text{partial}} = .19$. Paired-sample t-tests revealed a significant difference in N170 amplitude between upright and inverted faces for the extraversion group, $t(13) = 4.43$, $p = .001$, but no significant difference for the introversion group. Gamma analyses in progress reveal right-lateralized frontal/posterior coherence around 270 ms post-

stimulus onset. We predict significantly greater synchrony in this time window in extroverted individuals.

Conclusions: Results reflect the influence of social drive on face perception in typical development. This is the first study to demonstrate association between evoked gamma synchrony to faces and social personality traits. These findings parallel relationships observed in ASD and are consistent with the predictions of social motivation models of ASD.

123.004 4 Modulatory Effect of Context On Face Processing in Children with ASD. M. Coffman^{*1}, S. Shultz², W. Jones³, A. Klin³ and J. C. McPartland¹, (1)*Yale Child Study Center*, (2)*Yale University*, (3)*Marcus Autism Center, Children's Healthcare of Atlanta & Emory University School of Medicine*

Background:

Atypical neural response to human faces in autism spectrum disorders (ASD) has been hypothesized to develop from reduced social drive and consequent inattention to faces. Face perception is indexed by specific markers of hemodynamic (fusiform gyrus) and electrophysiological (N170) activity. Face-sensitive brain regions are demonstrated to activate when faces are merely implied by context, suggesting that intrinsic facial features are not necessary to evoke face-specific neural responses and that face-related activity is modulated by top-down processes, such as sensitivity to contextual cues. Given the limited temporal resolution of hemodynamic neuroimaging, it is not known whether the influence of context is exerted at early stages of face processing or at later stages, driven by feedback from higher cortical regions. Furthermore, individuals with ASD are noted to exhibit both behavioral and neural anomalies in face processing, but it is not known if and when these anomalies can be modulated by context.

Objectives:

Here we harness the temporal resolution of event-related potentials (ERPs) to (a) determine the stage of processing at which context exerts its influence on face processing and (b) examine neural mechanisms underlying the influence of context in children with ASD and typically developing (TD) children. We predicted that TD

children, but not those with ASD, would show contextual modulation of face-related activity at the earliest stages of face perception, as indexed by shorter latency ERP components (N170).

Methods:

Children with ASD (N=24; mean age=12) and matched TD children (N=24) participated in the study. EEG was recorded with a 256 electrode Geodesic Sensor Net while participants viewed: images of faces degraded such that internal features were no longer visible (DF1), followed by intact faces alone (faces) and further contextual cues disambiguating the degraded face (e.g., bodies with degraded faces), followed by a second set of degraded faces (DF2). Peak amplitude and latency were extracted for the N170 from electrodes over occipitotemporal scalp. To examine the effect of context on face perception, analyses contrasted N170 responses to faces to and degraded faces prior to and subsequent to establishing social context (DF1 and DF2, respectively).

Results:

A main effect of condition ($p < .001$) indicated that both groups displayed enhanced N170 amplitude to DF2 relative to DF1 ($p < .01$). N170 amplitude to faces was also greater than that elicited by DF1 ($p < .01$), but faces did not significantly differ from DF2. Children with ASD had significantly slower latency to DF1 and DF2 compared to TD ($ps < .05$).

Conclusions:

This study demonstrates that social context modulates face-related brain activity at early stages of face processing. Ambiguous stimuli, devoid of intrinsic facial features, elicited comparable response to faces only after exposure to intact faces. This modulation by social context was also observed in children with ASD. Consistent with prior research, although children with ASD showed an intact response in terms of signal strength, they displayed decreased processing efficiency, reflected in longer latencies to face-related ERP components. These findings suggest the potential value of treatments involving awareness of social context for children with ASD.

123.005 5 The Effect of Direct Gaze and Gaze Contingent Social Feedback On Attention Disengagement and RE-Engagement in Young Children with Autism. T. M. Helminen*, J. K. Hietanen, J. M. Leppänen and A. Kylliäinen, *University of Tampere*

Background:

According to previous studies on cued attention, toddlers with autism spectrum disorder (ASD) exhibit problems in holding attention to faces by showing faster attentional disengagement from faces compared to developmentally delayed or typically developing toddlers (Chawarska, Volkmar & Klin, 2010). However, it is not clear what kind of a role direct gaze plays in this attention disengagement from faces in young children with or without autism. Also, it is not known how positive social feedback, e.g., gaze contingent smiling, affects attentional re-engagement to face stimuli.

Objectives:

The objectives of this study were to investigate if young children with ASD exhibit problems in holding attention to faces with direct gaze, and to investigate how social nonverbal feedback affects attentional re-engagement to faces.

Methods:

In this study, typically developing preschoolers and preschoolers with autism were shown a centrally presented neutral face with direct gaze or downcast gaze or a toy, followed by a distracter stimulus presented either to the left or right. Participants' eye movements were recorded by an eye tracker. When the participant re-engaged the face stimulus after detecting the distracter stimulus, the expression on the stimulus face changed into a smile (participant's gaze contingent smile) or the toy started to move.

Results:

Preliminary results of the eye tracking analysis (latency of disengagement and re-engagement, and probability of re-engagement to the central face) will be presented.

Conclusions:

The preliminary findings will be discussed in relation to current theories of gaze behavior difficulties in ASD.

123.006 6 Abnormalities in Early Visual Processing of Faces in Autism. C. van den Boomen*¹, J. J. Fahrenfort² and C. Kemner¹, (1)*Utrecht University*, (2)*University of Amsterdam*

Background: Abnormal face processing is an often-reported deficit in autism spectrum disorders (ASD). However, it is unknown whether this is due to abnormalities in face processing itself, or in visual processes preceding face perception. A suggested atypical visual process in ASD is visual segmentation, i.e. the integration of details into a global figure and segregation of this figure from its background. It is unknown at what moment in time, i.e. during initial visual processing, visual segmentation, or object processing, abnormalities in visual processing of faces in ASD are firstly present.

Objectives: The current study investigated three processes involved in face perception: initial visual processing, visual segmentation and object processing. Using electroencephalography (EEG), it was studied which of these visual processing stages are abnormal in persons with ASD.

Methods: Adults with ASD and controls viewed three types of stimuli, while brain activity was recorded using EEG: orientation-defined textured faces, houses, and homogeneous stimuli. Stimuli were presented for a short duration, which is previously shown to evoke multiple ERP peaks, associated with different visual processes. These include an initial negative peak for all stimuli at occipital and occipito-temporal sites, associated with initial visual processing. In addition, there is a visual segmentation peak (i.e. a difference between faces and houses versus homogeneous stimuli) at occipital electrodes, and a positive and negative peak at occipito-temporal electrodes associated with object processing of faces and houses. Differences between groups on latency and amplitude of these peaks were of interest in the current study.

Results: Preliminary results indicated abnormalities in initial visual processing at occipital and occipito-temporal sites: longer latencies were present for ASD than control subjects. A trend towards this longer latency was also present in visual segmentation but

interestingly not at later peaks at occipito-temporal sites. Differences between groups in peak-amplitude were also indicated at occipito-temporal sites in initial processing as well as the later negative peak, associated with object processing. No peak amplitude differences between groups were present for initial processing or visual segmentation at occipital electrodes.

Conclusions: These results indicate delayed and diminished initial visual processing in ASD, as well as delayed visual segmentation. However, this latency difference was not present at later time-points at occipito-temporal sites, associated with object processing. Object processing did however seem to be abnormal regarding peak amplitude in ASD. Together, these results show that already at an early stage visual processing is abnormal in ASD.

123.007 7 Alterations of Visual Spatial Frequency Tuning in Autism Spectrum Disorders. F. Pei* and A. M. Norcia, *Stanford University*

Background: There is accumulating evidence from psychophysiological studies that low-level visual processing is somehow affected in individuals with ASD (e.g. Jemel et al 2010; Koh et al. 2011). These findings are consistent with the idea that ASD involves functional alterations at early cortical or even pre-cortical levels. Abnormalities in early stages of sensory processing are of interest because they could lead to down-stream functional deficits important for the characterization of the disorder.

Objectives: Here, using Visual Evoked Potentials (VEPs), we aim to further explore how well spatial information is transmitted over a wide range of spatial frequencies, including those at the limit of visibility (visual acuity).

Methods: We recorded VEPs in ASD children between 5 and 17 years old and aged matched controls. The test stimulus was a vertical sine-grating presented at 80% contrast that underwent pattern reversal at a rate of 7.5 Hz. The grating was swept in spatial frequency from 2 to 30 cpd over 10 sec. trials. Responses were measured in the frequency domain at the 2nd and 4th harmonics of the 7.5 Hz stimulus frequency (15 and 30 Hz).

Results: VEP response between 18 and 30 cpd and the corresponding grating acuity threshold did not differ between control and ASD participants, consistent with behavioral reports of a lack of superior spatial resolution in ASD. However, the second harmonic response at 2 to 18 cpd was significantly depressed in ASD relative to controls. On the other end, the second harmonic responses at 2 cpd and at all spatial frequencies for the fourth harmonic were normal. Thus, the ASD response is abnormal over a very limited and specific set of medium spatial frequencies for a particular temporal frequency of the response.

Conclusions: Although the present data cannot determine the anatomical substrate for the altered pattern reversal VEP response, they suggest that a highly specific substrate within early, possibly pre-cortical parts of the visual pathway must be involved. Substantial portions of the spatial frequency spectrum and the entire fourth harmonic response were completely normal, ruling out attention or other task demand differences between groups as an explanation.

123.008 8 Exploring Integrative Weaknesses in Verbal Adults with ASD: Behavioural Data Supported by EEG. M. Stothers*¹ and J. Oram Cardy², (1)*The University of Western Ontario*, (2)*Western University, Canada*

Background:

Adults with ASD who do not also demonstrate language impairment generally obtain average or better vocabulary scores on standardized testing (Stothers & Oram Cardy, 2012). Evident semantic weaknesses are described as pragmatic or social in nature, but this group of adults with ASD also have difficulty with academic, non-social language tasks. The present study examined the possibility that semantic difficulties arise during the integration of unique semantic representations.

Semantic integration involves the detection and elaboration of overlap between discrete representations to form a novel, higher-order relationship. As such, it is a form of gestalt perception – a relational process in which meaningful wholes are constructed from stimulus fragments that differ qualitatively from the larger whole. Low scores on nonverbal tests of gestalt perception have been reported in ASD, as has difficulty understanding verbal gestalts such as metaphors.

Objectives:

Objectives were to test the hypotheses that: a) adults with ASD without an accompanying language impairment nonetheless demonstrate weaknesses on tests that require the creation of a linguistic gestalt (e.g., hot + dog = food), b) such weaknesses affect the apprehension of both verbal and nonverbal gestalts, and c) reduced capacity for integrative processing in adults with ASD are evident in both cognitive and EEG data.

Methods:

Adults with a typical developmental history were compared to adults with a community diagnosis of ASD on baseline measures of vocabulary, as well as semantic integration and nonverbal gestalt perception. Measures of semantic integration included remote associate problems (swiss, cottage, cake = cheese), Similarities (how are two objects or concepts alike?), and metaphor identification. Nonverbal tests included Block Design, a baseline measure of visual-spatial skill, as well as puzzle assembly, gestalt closure, and object identification. EEG data was collected during metaphor and object identification.

Results:

1) Adults with ASD had lower scores for language tests that required integration than their peers without ASD. 2) Similar results were obtained for nonverbal integration tests, and verbal and nonverbal gestalt perception scores were positively correlated across the sample. 3) Behavioural results were supported by differences in waveform latency and amplitude in participants with ASD and without.

Conclusions:

ASD adults demonstrated low scores for verbal tests that required integration of unique semantic representations, and for nonverbal measures in which a novel whole had to be produced from unlike parts. Results could not be explained by differences in single word knowledge, nor by differences in visual-spatial ability as measured by Block Design; groups were not significantly different on either baseline measure. Time-locked responses to stimuli that required the formation of

gestalts during EEG data collection were delayed for participants with ASD. Results supported the hypotheses that verbal semantic integration and nonverbal gestalt perception rely on a common set of processes, and a weakness in gestalt perception distinguishes adults with ASD from their typical peers.

123.009 9 Impaired Feature Integration in Autism Spectrum Disorders Across Visual Hemifields. I. A. Peiker*, N. David, T. Schneider, D. Schöttle and A. K. Engel, *University Medical Center Hamburg-Eppendorf*

Background: The integration of visual details into a holistic percept is essential for object recognition. As this cognitive process seems to be impaired in people with autism spectrum disorders (ASD), autism might reflect a disorder of information integration. At the neural level, disrupted communication between brain areas could account for the cognitive deficits. In fact, altered connectivity has been reported in ASD, especially for interhemispheric communication.

Objectives: We sought to address whether connectivity is disturbed within or across cerebral hemispheres. Therefore, we employed the "slitviewing paradigm" which probes visuotemporal integration in an object identification task. A previous study using this paradigm showed lower performance of ASD individuals compared to a control group, but did not directly address altered connectivity as underlying pathology.

Methods: 20 adults with ASD and 20 control individuals matched for gender and age participated in the MEG-study. Participants viewed images of objects passing behind a vertical or horizontal slit and were asked to name the object they identified. Only fragments of the objects were visible at a given moment and thus had to be integrated over time. The horizontal slit, in contrast to its vertical counterpart, was intended to require integration over both hemispheres. MEG was recorded to investigate oscillatory neuronal activity from both hemispheres during the integration process.

Results: Behavioral data showed a significant interaction between group and the orientation of the slit. That is, participants with ASD were less accurate identifying objects presented behind a horizontal versus vertical slit, while controls did

not show such a performance difference between slit-conditions. The behavioral interaction was paralleled by an interaction at the neurophysiological level. Specifically, spectral power in the gamma band (at 80 Hz) was increased in the condition with the horizontal compared to the vertical slit within the ASD-group at central sensors, while it was not statistically different within the control group. In contrast, controls showed a condition effect at occipital sensors in lower frequencies, extending from theta to lower beta bands.

Conclusions: The oscillatory activity pattern implies different underlying brain processes with respect to visual feature integration in ASD compared to controls. In favor of our hypothesis, our findings might reflect reduced communication across cerebral hemispheres. As in real-world contexts stimuli regularly appear in both hemifields this finding is strongly relevant for the understanding of visual perception in autism.

123.010 10 Inhibitory Function Related to Tactile Processing Is Impaired in Children with ASD. N. A. Puts*¹, T. Koriakin¹, E. L. Wodka¹, M. Tommerdahl², S. H. Mostofsky¹ and R. A. Edden¹, (1)*Kennedy Krieger Institute*, (2)*University of North Carolina*

Background:

Impaired sensory processing is a common but poorly understood aspect of the behavioral traits of Autism Spectrum Disorder (ASD). Recent work suggests that a deficit in cortical inhibitory transmission may underlie some impairments in sensory processing. To date, no studies have shown that changes in neurochemical measures of cortical inhibition (e.g. GABA concentration) are related to behavior targeting the inhibitory system. In this study we combine tactile psychophysics and non-invasive measurements of the inhibitory neurotransmitter GABA (using Magnetic Resonance Spectroscopy; MRS) to investigate atypical touch sensitivity in ASD.

Objectives:

We tested two related hypotheses: (1) TDC and ASD pediatric populations differ in their response to tactile stimuli, which can be characterized by an absence of adaptation mechanisms (through GABA-B-ergic processes) in children with ASD. (2)

This difference in tactile processing can be partly attributed to decreased levels of GABA within the sensorimotor cortex.

Methods:

Behaviour: 17 typically developing children (TDC) and 6 children diagnosed with ASD (ages 8-12) participated (2 female, all right-handed). Subject and parental consent was obtained under the approval of the IRB at Johns Hopkins University and the Kennedy Krieger Institute. *Behavioural:* All participants received a battery of vibrotactile tasks. Children performed (1) a static and a dynamic threshold task (stimulus frequency: 25 Hz). (2) Three 2-alternative forced choice (2AFC) amplitude discrimination tasks (no adaptation, single site adaptation & dual site adaptation; 500 ms, 25 Hz, starting amplitudes 100 & 200 μ) (3) Sequential and simultaneous frequency discrimination tasks (starting frequency 30 & 40 Hz). *Neuroimaging:* Edited MRS measurements of GABA were made in a 'sensorimotor' volume centred on the right motor hand-area for 5 participants in each group. All scanning was carried out on a Philips 3T MRI-scanner. GABA concentration in was quantified from the ratio of the integral of the edited GABA signal to the integral of the unsuppressed water signal from the same volume.

Results:

Static detection threshold was significantly lower than dynamic detection threshold in TDCs ($p < 0.02$), but not the ASD group ($p > 0.2$). Amplitude discrimination increased after single-site adaptation compared to no-adaptation in the TDC group ($p < 0.01$), but not in the ASD group ($p > 0.5$). There were no significant differences in frequency discrimination performance between the two tasks or groups. There was a significant reduction in GABA concentration for the ASD group compared to TDCs ($p < 0.05$). In addition, preliminary analysis shows a correlation between GABA concentration and frequency discrimination in the TDC group ($R = -0.67$, $p < 0.05$; also see Puts et al., 2011), but this correlation is absent in the ASD group ($R = 0.26$, $p > 0.5$).

Conclusions:

Our preliminary behavioural results replicate previous findings and when taken with our MRS findings we interpret our data to be consistent with the presence of reduced GABAergic-mediated inhibition in this population. Analysis of the behavioural data suggests that mechanisms underlying adaptation are impaired in ASD, and these are potentially GABA-B-ergic related and the absence of a correlation between GABA and frequency discrimination in ASD suggests this as well.

123.011 11 Voice Processing and Language Impairment in Children with ASD. N. Bruneau^{*1}, O. Rogier², C. Barthélémy¹ and F. Bonnet-Brilhault³, (1)INSERM U930, Université François Rabelais, CHRU de Tours, (2)Brain Mind Institute, (3)UMR Inserm U930

Background: Development of oral language and communication is based on adequate speech perception which is closely embedded with voice processing. Previous fMRI studies showed that adults with ASD fail to show voice-selective activity in the "temporal voice areas" localized in the superior temporal sulcus despite a normal response to nonvocal sounds. No data are available in children. Investigating development of voice processing would therefore be of interest for better understanding of neurophysiological impairments underlying communication disorders and/or language impairment in ASD.

Objectives: The aim of the present study was to investigate the electrophysiological correlates of voice processing in 4- to 12-year-old children with ASD compared to typically developing children. Voice processing was evaluated by comparing cortical auditory evoked potentials (AEPs) to vocal sounds vs. environmental sounds (non-vocal) of everyday life. Pattern of response were assessed according to verbal abilities in children with ASD.

Methods: Participants were 50 typically-developing (TD) children and 12 children with ASD, all aged 4 to 12 years. The stimuli used were extracted from the sequences used in Belin et al.'s block-design fMRI studies with stimulus duration adjusted to 500 ms. AEPs were analyzed topographically (scalp potential and current density mapping). Mean (\pm sem) verbal and non-verbal IQ scores of children with ASD were 69 ± 14 and 87 ± 11 respectively.

Results: A specific response to voice was found in TD children as a positive deflection localized over right fronto-temporal sites, which we termed Fronto-Temporal Positivity to Voice (FTPV), with maximal amplitude in the 100-250 ms latency range. This response was very robust throughout childhood. It was identical in the 4 age-groups: 4-5, 6-7, 8-9, 10-12 year-olds. Compared to age-matched TD children, FTPV amplitude was significantly smaller in children with ASD who had concomitant language impairment whereas it was greater in children whose verbal abilities were less affected.

Conclusions: The fronto-temporal positivity to voice (FTPV) recorded in TD children may constitute the electrophysiological counterpart of the activation of the temporal voice areas previously described in neuroimaging studies. Results in children with ASD indicated atypical responses to voice. Moreover the relationship between voice processing and verbal abilities lead us to hypothesize that cortical response to voice is a putative predictive marker of language development in ASD.

123.012 12 The Development of Contour Completion Processes Across Childhood and Adolescence in Autism Spectrum Disorders. T. S. Alschuler^{*1}, S. Molholm², A. C. Snyder², A. B. Brandwein³, N. Russo⁴, H. Gomes⁵ and J. J. Foxe², (1)*The Graduate Center - City University of New York*, (2)*The Sheryl and Daniel R. Tishman Cognitive Neurophysiology Laboratory, Albert Einstein College of Medicine*, (3)*The Graduate Center and Queens College of the City University of New York*, (4)*Syracuse university*, (5)*City College of New York*

Background: Autism spectrum disorders (ASDs) are currently diagnosed via observation of complex behaviors such as social impairment and restricted interests. However, there is also indication that atypicalities at more basic levels of processing may play a role. The visual system in healthy adults and children is known to automatically "complete" contours given partial information, in essence making parts into wholes. Neuropsychological tests suggest that in autism there is a tendency to default to processing parts of objects rather than the whole, indicating that there might be a deficit in early and automatic integration processes.

Objectives: Here we used well-characterized electrophysiological assays of automatic contour

completion to test whether a tendency toward the local, a characteristic of the autism phenotype, might originate in deficits in early automatic contour completion processes.

Methods: A common approach to understanding completion processes uses stimuli with incomplete contours that induce perception of complete contours –illusory contour (IC) stimuli (Kanizsa 1976). These are useful because rearrangement of elements of identical stimulus energy gives rise to different percepts. In the illusion-inducing configuration, continuous contours appear to form a two-dimensional object. In the non-inducing arrangement only the inducers are typically perceived. Robust modulation as a function of IC status of the visually-evoked potential (VEP) provides an index of the neural contributions underlying this perceptual change (Murray et al. 2002).

ERPs to IC and non-IC stimuli were compared between children with a diagnosis of ASD and their neurotypical counterparts, in three age cohorts: 6-9, 10-12, and 13-17. IC-inducing stimuli were presented at three spatial extents (4, 7 and 10 degrees). Participants performed an unrelated task. IC-effect amplitudes and latencies were measured for two well-characterized modulations of the VEP associated with perceptual completion: The IC-effect, occurring during the N1 timeframe (~100-200 ms) and associated with automatic filling-in of boundaries (Shpaner et al. 2009) and the N_{cl} , occurring between ~250-400 ms, reflecting more effortful visual object processing

Results: In typically developing controls, across all age-groups, modulation of the ERP as a function of IC status was observed in the N1-timeframe. This was followed by N_{cl} modulation that was greatest for the two younger groups. Spatial extent of the inducers did not influence contour integration processes in any age-group. In the ASD group, contour completion processes were less robust across age groups and across the manipulation of spatial extent, suggesting greater inter-subject variability in this group. Notably however, when IC-effects were present they were observed in both early and late timeframes.

Conclusions: In the ASD cohort we find greater variability in the automatic completion of visual

information, as indexed by IC-effects. Data will be further analyzed to determine if there is a bimodal distribution within this group whereby some individuals show automatic contour completion and others do not, and whether this correlates with an index of ASD phenotype.

123.013 13 Early-Stage Visual Processing Abnormalities in Children with ASD and Unaffected Siblings. P. M. Weinger^{*1}, V. Zemon¹, J. Gordon² and L. Soorya³, (1)*Yeshiva University*, (2)*Hunter College*, (3)*Rush University*

Background: Previous studies have described atypical perceptual processing in children with ASD, as well as a high prevalence of sensory symptomatology. However, the early stages of sensory processing, specifically within the visual cortex, remain underexplored. Quantitative and objective measures can be obtained through noninvasive electrophysiological testing based on extracting the visual evoked potential (VEP) from the ongoing electroencephalogram (EEG). These measures may elucidate underlying neural correlates of ASD and they offer the capability to track neural development and monitor the effects of treatment.

Objectives: (1) To develop and implement a battery of short-duration neurophysiological tests that can be used to assess the integrity of visual pathways in children with ASD, and (2) to examine differences in the visual pathways of children with ASD, unaffected siblings and typically developing controls.

Methods: Transient and steady-state VEP recordings were obtained from 11 children with ASD ($M_{age} = 9.09$, $SD = 2.34$), 12 control participants ($M_{age} = 7.17$, $SD = 2.56$), and 5 unaffected siblings ($M_{age} = 6.00$; $SD = 1.58$) using the Neucodia system (VeriSci Corp.). In short-duration runs, each stimulus condition was presented for ~ 2 s and the EEG was recorded synchronized to the display's frame rate. Stimulus conditions (10-deg field, mean/background luminance = 50 cd/m²) included a contrast-reversing checkerboard (100% contrast) to elicit transient VEPs (tVEP), used to examine multiple frequency mechanisms, a pair of radial patterns (partial-windmill and windmill-dartboard) with elements contrast-reversed at ~ 4 Hz (32% contrast) to elicit steady-state VEPs (ssVEP), used to quantify direct-through excitatory and lateral inhibitory contributions to the response, and a

dartboard with each element contrast-reversed by a sum of high frequency sinusoids (22.8 & 24.8 Hz, 32% contrast/sinusoid) to yield an intermodulation response at 2 Hz that reflects excitatory nonlinear interactions. In addition, contrast-sweep conditions (bright or dark isolated checks) in which contrast increased in octave steps from 2-64% elicited ssVEPs at 12.5 Hz to assess ON/OFF pathways, respectively. ASD diagnoses were determined based on research diagnostic instruments (ADOS, ADI-R) and DSM-IV-TR criteria.

Results: Differential effects were observed across stimulus conditions. Children with ASD and unaffected siblings both displayed deficits in low contrast responses, particularly under conditions that emphasize contributions from the magnocellular pathway. Increased neural noise was also observed in both the ASD and unaffected sibling groups. In contrast, the ASD group displayed evidence of strong GABA-ergic inhibition and enhanced short-range lateral interactions. No differences were observed in the excitatory contributions to the VEP in response to the two-sinusoid condition.

Conclusions: The use of low-level, non-social, stimuli provide evidence for both enhanced and weakened visual processing in the early visual pathways of children with ASD and unaffected siblings. Further studies are needed to examine whether these differences persist in larger samples and in more specific age cohorts. Short-duration VEPs hold promise as a rapid and reliable method to examine electrophysiological biomarkers, or endophenotypes, of ASD. Findings also demonstrate that short-duration stimuli, in conjunction with multivariate statistical analysis of the brain's responses, can yield sensitive and objective indices of particular neural pathways.

123.014 14 An ERP Investigation of the Acoustic Change Complex in High-Functioning ASD. A. Bhatara^{*1}, T. Babikian², E. Laugeson³, R. Tachdjian², E. Ballat² and Y. S. Sininger², (1)*Université Paris Descartes*, (2)*UCLA*, (3)*UCLA Semel Institute for Neuroscience & Human Behavior*

Background: There is a growing body of evidence showing abnormalities in the auditory system of individuals with autism spectrum disorders (ASD). ERP studies examining auditory evoked responses in individuals with ASD have shown evidence of atypical lateralization and

maturational patterns as well as increased sensitivity to changes in sound (Bomba & Pang, 2004). Auditory change detection has been investigated using paradigms that elicit a mismatch negativity (Gomot et al., 2011), but to our knowledge, no study on ASD has examined the acoustic change complex, which is elicited by changes in frequency or a silent gap (Martin & Boothroyd, 1999).

Objectives: To investigate the acoustic change complex in adolescents with high-functioning ASD.

Methods: Fifteen adolescents aged 10-14 with high-functioning ASD and 16 age-matched typically developing (TD) controls listened passively to auditory stimuli with changes while cortical responses were measured using a 21-channel EEG cap. Stimuli were 1500 ms tones or noise presented monaurally, consisting of an onset stimulus lasting 700 ms followed by either a 50% frequency change (Task 1) or a 20-ms gap of silence (Task 2). Stimuli in Task 1 were tones of 500 or 4000 Hz and in Task 2 were tones of 1000 Hz or broadband noise. Frequency and ear of presentation were randomized within tasks, and tasks were counterbalanced. Each task continued until 150 trials for each frequency/ear combination were accepted. Peak measurements (amplitude and latency) were performed for the N1b wave at the vertex (Cz and Fz) and the T-complex at the temporal electrodes (T7 and T8), described here as N1a and N1c with a positive Ta between them.

Results: In Task 1 (Frequency), there was a group by ear interaction ($p = .047$): Whereas the ASD group showed a shorter latency N1a at the change in response to sounds presented to the left ear (LE) than to the right ear (RE), the TD group showed the reverse pattern. Relative to the TD group, the ASD group also showed higher amplitude N1a peaks ($p = .005$) and shorter latency of the Ta component ($p = .047$) implying increased sensitivity to the change. In Task 2 (Gap), at the onset of the stimuli, the TD group showed higher amplitude N1a peaks recorded at the left (T7) than at the right (T8) temporal electrode ($p = .001$), but the ASD group showed no difference between electrodes ($p = .96$). Also, the ASD group showed shorter latencies than the TD group for the Ta peak ($p = .02$) and higher

amplitudes for N1b ($p = .04$). After the gap, the N1b peak had shorter LE latencies for the ASD group ($p = .01$), whereas the TD group showed no ear difference ($p = .6$).

Conclusions: The ASD group showed evidence of atypical laterality, evidenced by both ear and electrode differences. In addition, increased amplitude and shortened latencies suggest increased sensitivity to change in the ASD group. Along with previous work, this supports the hypothesis that difficulties with language and nonverbal communication may have bases in atypical low-level auditory processing.

123.015 15 Atypical ERP Effects During Auditory Processing in Children with Autism Spectrum Disorder. S. E. Schipul^{*1}, F. C. Donkers², G. T. Baranek¹, K. M. Cleary¹ and A. Belger¹, (1)University of North Carolina at Chapel Hill, (2)Tilburg University

Background: Unusual sensory experiences have been reported in a large percentage of individuals with autism. While behavioral characteristics of sensory processing have been well documented, less is known about their neurobiological correlates. Electroencephalography (EEG) studies enable the analysis of different time-locked components of sensory processing, and may elucidate the temporal characteristics of aberrant sensory processing in individuals with autism.

Objectives: The current study measured event-related potential (ERP) effects during an auditory oddball task in young children with autism, in order to examine the sensory, perceptual, and cognitive processing of auditory information in the disorder.

Methods: Participants include children with autism spectrum disorder (ASD), children with other developmental disabilities (DD), and neurotypically developing children (NT), between 4 and 12 years of age, with a mean age of 7. ERPs were collected during a passive listening task, during which participants watched a video of their choice, while ignoring sounds played over speakers. The stimuli consisted of 2200 standard tones, 100 duration deviant tones, 100 pitch deviant tones, and 100 novel sounds, randomly presented. 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 and mismatch negativity - MMN, reflecting pre-attentive perceptual processes; and (3) the P3a, reflecting post-sensory attentional processes.

Results: Preliminary results with 36 in the ASD group and 41 in the NT group suggest that children with ASD have an attenuated response to novel sounds. The P3a response for the comparison of novel sounds to standard sounds was significantly smaller in ASD. This component of the neural signal occurs relatively late (around 300 ms) and indicates post-sensory involuntary attention. Therefore, this finding suggests that the children with ASD show evidence of reduced attentional orienting to novel sounds in this passive listening paradigm. The children with ASD also had a smaller amplitude for the N1 for standard sounds, reflecting atypical pre-attentive perceptual processes even for standard, repeated tones.

Conclusions: These preliminary findings suggest atypical electrophysiology responses to sensory stimuli in children with ASD, particularly in the P3a. This may reflect abnormal attentional orienting to environmental novel stimuli, consistent with the prevalence of aberrant sensory sensitivities in many children with autism. Further analyses will include the developmental disabilities participant group to determine if these neural characteristics are specific to ASD. We will also examine relations between these ERP components and clinical sensory features in the participants with ASD.

123.016 16 Missing and Delayed Auditory Responses in Young and Older Children with Autism Spectrum Disorders. J. C. Edgar^{*}, M. R. Lanza, J. F. Monroe, S. Y. Khan, L. Blaskey, K. M. Cannon, J. Jenkins, S. Qasmieh, S. E. Levy and T. P. Roberts, *Children's Hospital of Philadelphia*

Background: During development, the latency of the 50ms and 100ms auditory response decreases as a function of age. Individuals with autism spectrum disorders (ASD) have delayed and even sometimes missing 100ms auditory responses.

Objectives: The present study examined the development of left and right superior temporal gyrus (STG) 50ms (M50) and 100ms (M100) auditory responses in typically developing children (TD) and in children with ASD. It was hypothesized that (1) left and right STG M50

responses would be observed equally often in younger than older children, (2) left and right M100 responses would be observed more often in older than younger children indicating later development of secondary auditory areas, and (3) M100 but not M50 would be observed less often in ASD than TD in both age groups, reflecting slower development of later developing auditory areas in ASD.

Methods: 35 controls, 63 ASD without LI (ASD-LI), and 38 ASD with LI (ASD+LI) were recruited. Binaural tones were presented. Using single-dipole source localization, the presence or absence of a STG M50, M100, and M200 was scored. A median split separated subjects into younger (6 to 10-years-old) and older groups (11 to 15-years-old).

Results: Although M50 responses were observed equally often in older and younger subjects and equally often in TD and ASD, M50 responses were delayed in ASD-LI and ASD+LI bilaterally. For M100, an effect of age was observed only in ASD-LI (young =76%, older = 95%; $p=0.01$). In contrast, left and right STG M100 responses were observed in almost all young and old TD subjects, and left and right STG M100 responses observed less frequently in young and old ASD+LI. Group comparisons showed that in younger subjects, M100 responses were observed more often in TD than ASD+LI (90% vs 66%, $p=0.04$), with no differences between TD and ASD-LI (90% vs 76% $p=0.14$) or between ASD-LI and ASD+LI (76% vs 66%, $p=0.53$). In older subjects, whereas no differences were observed between TD and ASD+LI (91% vs 75%, $p=0.24$), responses were observed more often in ASD-LI than ASD+LI (95% vs 75%, $p=0.03$). Given similar differences between TD versus ASD+LI and ASD-LI versus ASD+LI, the non-significant TD versus ASD+LI finding is likely due to a smaller N in the TD group.

Conclusions: TD subjects have an identifiable left and right M50 and M100 by 6 years of age. Although M50 responses were present in all groups, M50 responses were temporally delayed in ASD, suggested delayed development of primary auditory areas. Whereas there was a significant increase in the presence of M100 responses in older than younger ASD-LI, many older ASD+LI subjects continued to have a

missing M100. Examining the TD data, present findings indicated that by 11 years a right M100 should be observed in 100% of subjects and a left M100 in 80% of subjects. Thus, by 11years, lack of a left and especially right M100 offers neurobiological insight into abnormal sensory processing that may underlie language or cognitive impairment.

123.017 17 Neurophysiological Evaluation of Acoustic Startle Response in Japanese Children with Autism Spectrum Disorders. H. Takahashi*, T. Nakahachi, A. Moriwaki, R. Takei, K. Ogino, Y. Iida, N. Inada and Y. Kamio, *National Center of Neurology and Psychiatry, Japan, National Institute of Mental Health*

Background: Acoustic startle modulation, including prepulse inhibition (PPI), is considered to be one of the most promising neurophysiological index for translational research in psychiatry. However, as for autistic spectrum disorders (ASD), startle modulation was not consistent through children to adults: adults with ASD presented PPI impairment, on the other hand, children with ASD did not. Above all, basic ASR profile of ASD is not known well. People with ASD is known to have enhanced auditory perception, however, ASR to weak stimuli in ASD is not investigated well. Recently, children with ASD are reported to have prolonged startle latency. And, in addition, basic ASR profile, such as startle magnitude, is known to differ across races. Thus, basic ASR profile, including startle magnitude, especially to weak stimuli, and startle latency, should be investigated across races.

Objectives: To evaluate the basic ASR profile, including peak startle latency, startle magnitude to weaker stimuli, in Japanese children with ASD and typical development (TD), and, to evaluate their relationship to ASD characteristics

Methods: Ten Japanese children with ASD and 34 Japanese children with TD participated in this study. The electromyographic activity of the left orbicularis oculi muscle to acoustic stimuli of 65 to 115 dB SPL, in increments of 5 dB, was measured to evaluate ASR. Average eyeblink magnitude, average peak startle latency of ASR for each acoustic stimuli intensity was evaluated. The Electroencephalography (EEG) was also recorded during the testing. Based on the electric potential distribution of ERP 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. ASD characteristics of all subjects were assessed by Social Responsive Scale (SRS).

Results: Compared to TD, ASD group showed significantly larger startle magnitude to weak acoustic stimuli of 65, 70, and 80 dB. Peak startle latency was prolonged in children with ASD compared to TD. Startle magnitude to weak acoustic stimuli of 65dB, 70dB, 75dB, and, 80dB correlated negatively to T score of SRS Social Awareness subscale. Peak startle latency correlated with T score of SRS total score and SRS subscale of Social Awareness, Social Cognition, Social Communication, and, Autistic Mannerisms. EEG current source density was widely distributed across brain areas in TD, however, was restricted mostly in frontal region in ASD.

Conclusions: Larger startle magnitude to weak stimuli and prolonged peak startle latency were related to several aspects of ASD characteristics. Brain activity involved in the mechanism of ASR was atypical in ASD. Our results suggest that comprehensive investigation of ASR, including startle magnitude to weak stimuli, peak startle latency, might contribute to uncover the impairment of the neural circuitry in autism.

123.018 18 Otoacoustic Emissions and Efferent Feedback in ASD.

A. E. Luebke^{*1}, P. D. Allen¹, J. DeSanctis², R. M. Nelson², A. Lord² and L. Bennetto², (1)University of Rochester Medical Center, (2)University of Rochester

Background: Filtering auditory information in background noise is required for a person's social communication abilities, and impairment of such filtering abilities is one of the key features of autism spectrum disorders (ASD). A potential physiological basis for filtering relevant auditory information is caused by descending regulation by the brain onto cochlear activity—the olivocochlear efferent feedback systems. The olivocochlear efferent systems consist of two components whose cell bodies are found in the superior olivary complex: a medial olivocochlear (MOC) system projecting primarily to cochlear outer hair cells (OHCs); and a lateral olivocochlear (LOC) system projecting primarily to the dendrites of cochlear afferent neurons in the region beneath inner hair cells. The contractile activity of the OHCs can be evaluated in human subjects, because

contractions of the OHCs generate acoustic signals (otoacoustic emissions; OAEs), which can be recorded in the external ear canal, making it possible to directly measure auditory filtering processes at the cochlear periphery. It has previously been shown that adolescents and children with ASD have reduced MOC efferent feedback strength using transient OAEs (TrOAEs) and greater asymmetries in their responses (right vs. left ear) when compared with typical controls. Additionally, when brains have been examined from adults with ASD (using autopsy or MRI), the superior olivary complex was found to be either absent, greatly reduced, or disorganized when compared with age-matched control brains, again suggesting that the olivocochlear region is affected in individuals with ASD.

Objectives: Our objective was to specifically measure efferent feedback strength and baseline otoacoustic emissions in children with ASD when compared with matched, typically developing controls.

Methods: Children with ASD (n=25) and typically developing controls (n=26), ages 6 through 17, participated in this study. Groups were rigorously characterized via ADI-R and ADOS, and matched on age, gender, and verbal ability. Exclusion criteria included diagnoses of neurological or genetic disorders, and other conditions or illnesses that could affect hearing. Hearing was evaluated via audiometry; all subjects had thresholds below 20 dB SPL for 500, 1000, 2000, and 4000 Hz, and <25 dB SPL for 8000 Hz. To perform the measurement of cochlear efferent feedback strength and baseline otoacoustic measures, we tested right and left ears of all subjects in a sound attenuated room, with i) baseline DPOAE (distortion-product) and TrOAE (transient) conditions (without binaural broadband noise stimulation); then ii) TrOAEs with broadband suppression (400-750 ms).

Results: High-functioning children and adolescents with ASD have greatly reduced DPOAE responses in the 1-2 kHz speech frequency range (~8dB SPL, f₂=1 kHz, p<0.001), yet have comparable DPOAE responses at 0.5 and 4-8 kHz regions. The analysis of the spectral features of the TrOAE baseline and efferent measures are underway, but expect these measures to be similarly reduced in ASD.

Conclusions: Non-invasive measures of cochlear function and efferent feedback strength may serve as an early physiological biomarker for ASD.

Treatment Trials: Behavioral Interventions Program

124 Treatments: Early Intervention Trials

This session includes trials investigating a range of early intervention methodologies.

124.019 19 Changes in Rates of Development for Preschool Children with ASD in Two Comprehensive Treatment Programs. S. Odom*¹, K. Hume² and B. Boyd³, (1)*University of North Carolina*, (2)*University of North Carolina, Chapel Hill*, (3)*University of North Carolina at Chapel Hill*

Background: A range of comprehensive treatment models (CTMs) have been developed for preschool children with ASD (Odom, Boyd, Hall, & Hume, 2010), but to date there have been few comparative treatment studies of such models. The TEACCH and LEAP are two comprehensive treatment models (CTMs) with a long-standing history in the field of autism and that are based on different theoretical frameworks. In an initial study, significant development effects across time occurred for children in both models and in a high quality eclectic comparison set of classrooms with few between group differences (Boyd, Hume... Odom, 2012). However this analysis did not control for the possible effects due to maturation.

Objectives: The objective of the current analysis was to examine differential changes in the rates of development as compared to pre-enrollment rates of development for preschool children with ASD enrolled in TEACCH, LEAP, and a high quality eclectic condition.

Methods: A rigorous, quasi-experimental study involving n = 75 classrooms meeting inclusion criteria of high fidelity and quality (28 BAU, 22 LEAP, 25 TEACCH) and involving 205 children with ASD. The Mullen Early Scales of Learning, the Preschool Language Scales (PLS), and the Vineland Adaptive Behavior Scale were collected on children at the beginning and end of children's first year in intervention. Proportional Change Indices (PCI; Wolery 1983) were used to analyze rate of growth previous to the onset of the intervention to the rate of growth during the intervention. PCIs < 1 indicate that growth was slower while in intervention, =1 indicate that the rate of change was the same before and during

intervention, and >1 indicate that the rate of growth of accelerated while enrolled in intervention.

Preliminary Results: Data analysis is ongoing, and will include analysis of the Vineland scores, moderating variables, and group comparisons. Initial analyses indicate that students in all conditions exhibited substantial changes in rates of development relative to their pre-treatment rates of development on most measures. Children in TEACCH classrooms had the highest rate of change in expressive language as measured by the Mullen EL (1.42 TEACCH, 1.22 BAU., 98 LEAP) and PLS EC (2.06 TEACCH, 1.82 LEAP, 1.94 BAU) when compared to students in LEAP and BAU.

Measures of receptive language indicated varied results, with BAU students demonstrating greater growth on the Mullen RL (1.58 BAU, 1.47 LEAP, 1.28 TEACCH), and TEACCH students showing greatest growth on the PLS AC subscale (3.09 TEACCH, 1.97 LEAP, 1.85 BAU). Students in LEAP classrooms demonstrated the greatest rate of change on the fine motor skills (1.02 LEAP, .86 BAU, .76 TEACCH) and students in TEACCH classrooms had the highest rate of growth on the Mullen visual reception subscale (VR=1.69, 1.4 BAU, .82 LEAP).

Conclusions: In this preliminary analysis, the PCI scores indicate substantial growth above that which would be expected from pre-treatment rates of development on measures of receptive language, expressive language, and visual reception, with differential effects occurring on some measures. Subsequent analyses now occurring will determine moderator effects and significance of differential PCI growth measures.

124.020 20 Development and Evaluation of the Frankfurt Early Intervention Program. C. M. Freitag*, K. Teufel, J. Valerian, S. Feineis-Mathews and C. Wilker, *Goethe University*

Background:

The Frankfurt Early Intervention Program FFIP is a social pragmatic approach, which has been developed within the funding framework of public services in Germany. In FFIP, individual 2:1, behaviourally and developmentally based therapy with the child is combined with parent education and training of kindergarten teachers. Treatment frequency is 2 hrs / week. Methodological elements are classical, but highly individualised

ABA approaches for very young children, combined with visual structuring, incidental teaching and natural learning paradigms for older children and eventually social learning within a small group of two children.

Objectives:

We present 1- and 2-year follow up data on change in irritability, lethargy, stereotypy, hyperactivity, inappropriate behaviour and autistic symptoms.

Methods:

Seventeen children with a diagnosis of autism, Asperger Syndrome or atypical autism according to ICD-10, aged 2-7 years old were enrolled into the study. Diagnosis was made by ADI-R and ADOS. Autistic Symptoms were measured by the SRS, irritability, lethargy, stereotypy, hyperactivity, inappropriate behaviour were measured by the Aberrant Behavior Checklist. ABC and SRS measures after one year (t2) were obtained from 16, after two years (t3) from 12 children. Difference measures were studied for change from 0 by t-tests.

Results:

In the ABC, just a few behavioural changes were observed: A trend for a change in irritability was observed after two years of therapy (t3-t1; $p=0.064$), and hyperactivity decreased significantly after two years of therapy (t3-t1; $p=0.019$).

Autistic symptoms, as measured by the SRS, significantly decreased in the second year of therapy ($p=0.006$), but not in the first year ($p=0.945$); for t3-t1, a trend was observed ($p=0.079$).

Conclusions:

Behavioural changes by the FFIP were not strong, but autism symptoms clearly decreased in the second year of therapy. The decrease in hyperactivity may either be caused by age effects or by therapy. Currently, a control group is

collected to show the specific effects of the FFIP intervention.

124.021 21 Early Analysis of the Feasibility and Acceptability of Family Implemented Teacch for Toddlers (FITT). L. Turner-Brown^{*1}, K. Hume² and B. Boyd³, (1)*University of North Carolina*, (2)*University of North Carolina, Chapel Hill*, (3)*University of North Carolina at Chapel Hill*

Background:

Interventions based on the TEACCH model are widely accessible for children with ASD; however, there is limited evidence of the efficacy of the approach for young children with autism. FITT was developed as a structured teaching intervention adapted to be developmentally appropriate for toddlers with ASD, and more responsive to needs of families from a range of socioeconomic backgrounds. FITT is a 6-month intervention that includes 4 group-based parent education sessions and 20 in-home individualized coaching and feedback sessions from a trained therapist. The goals of FITT sessions address social-communication skills, play skills, prevention of problem behaviors, and positive home routines. Study of the efficacy of FITT on child and family outcomes is ongoing in a three-year randomized control trial.

Objectives:

The objectives of this early analysis are to (a) examine the feasibility of FITT through study of therapist implementation and parent adherence data, as well as parent attendance and session completion data, and (b) examine the acceptability of FITT through study of social validity measures.

Methods:

Participants include 11 toddlers with ASD between 17 and 35 months of age at enrollment, as well as their primary caregivers (all mothers). Only those toddlers randomly assigned to FITT are included in the present study. Treatment fidelity data were collected at 100% of sessions (IOA at approximately 15% of sessions), and parent adherence ratings were also collected at each session. Parents completed a social validity rating form upon completion of the 6-month intervention period. Social validity ratings covered 5 domains:

overall satisfaction, goals, procedures, perceived child outcomes, and parent outcomes. Items in each domain were rated using a Likert scale (1 – 5), with higher ratings associated with greater satisfaction.

Results:

Feasibility results were promising: attendance levels were excellent, with all participants completing all 20 in-home sessions during the 6-month period. Treatment fidelity ratings of project interventionists was strong, with average fidelity ratings of 93% (range: 68% - 100, Inter Observer Agreement ranging from 80% - 100%). Parent adherence to FITT was adequate but variable, with parents achieving an average of 74% of total possible adherence points (Range: 65% - 87%). Social validity ratings were high in all domains: satisfaction (mean = 4.8, s.d. = .3), goals (mean = 4.7, s.d. = .4), procedures (mean = 4.7, s.d. = .4), perceived child outcomes (mean = 4.8, s.d. = .4), and parent outcomes (mean = 4.7, s.d. = .5). Associations between social validity ratings and child outcomes will be explored.

Conclusions:

Results suggest that FITT is a feasible and acceptable parent training program for parents of toddlers with ASD as rated by parents and interventionists, and evidenced by parent completion and adherence to intervention practices. Strong parent ratings suggested parents felt the program was helping both them and their toddler, that the strategies were ones they would continue to use, and that the goals of the intervention were appropriate. Treatment fidelity for project interventionists was also high. Parent adherence ratings were more variable and factors associated with these ratings will be discussed.

124.022 22 Evaluating Social Communicative Behaviors Across Treatment Settings for Children with Autism. E. C. Worcester^{*1}, L. Schreibman¹ and A. Stahmer², (1)University of California, San Diego, (2)Rady Children's Hospital, San Diego

Background: Many intervention options for children with autism spectrum disorders (ASD) are widely available. The majority of research focuses on the effectiveness of interventions delivered

one-on-one by a trained therapist in the home and in specialized inclusive preschools. However, there has been a lack of research conducted on the direct comparison of different treatment delivery models.

Objectives: This study compares the acquisition of social skills in children at-risk for ASD enrolled in either an in-home one-on-one intervention program or an inclusive preschool program.

Methods: A total of 17 children, (mean age = 25 months) identified as at-risk for ASD were recruited from two early intervention programs. Nine children were recruited from a one-on-one in-home intervention program and the remaining eight children were recruited from an inclusive preschool. Both programs are public options for children under age three with ASD and staff from both programs were trained using similar behavioral and developmental strategies, reducing differences due to intervention types and highlighting the difference in intervention delivery; inclusive versus in-home. At intake chronological age, Early Learning Composite Score on the Mullen Scales of Early Learning, and score on the Social Domain of the Vineland Adaptive Behavior Scales were not significantly different between groups. Children were assessed within eight weeks of entering intervention and then again six months later. At each assessment period, children and parents participated in a battery of social skill assessments including the Early Social Communication Scales (ESCS), a structured play observation with a parent and another with a peer, and a video-referenced rating of early reciprocal social behavior (vrRSB) developed in the Constantino Laboratory at Washington University in St. Louis.

Results: A repeated measures ANOVA revealed significant decreases in parental ratings of social deficits on the vrRSB ($M_1=51.24$, $M_2=41.53$, $F=10.444$, $p=0.007$), and an increase in rate of initiating joint attention with the experimenter on the ESCS ($M_1=0.64$, $M_2=.91$, $F=4.92$, $p=.042$) across assessment periods for both groups of children. There were no differences over time or between groups in peer play or play with parents.

Conclusions: Generally, improvements in social skills across children were seen over time, although child performance was variable. Children

showed improvements in joint attention skills, and were rated as having fewer social deficits by their parents over time in both groups. These data indicate that early intervention delivered in one-on-one or inclusive settings can be effective in supporting social skill development in children at-risk for ASD. However, the lack of changes in play with peers and parents over time warrant further investigation. The lack of differences between programs highlights the need for the analysis of resources consumed by each program type and child characteristics that may predict differing outcomes in one service delivery setting over another.

124.023 23 Initial Results of a Continuous Intervention Program for Children with ASD. S. Kotsopoulos*¹, I. Florou¹, A. Georgiou¹, M. Gyftogianni¹, A. Kotsopoulos², G. Toulitatos¹ and A. Troupou¹, (1)*EPSYPEA*, (2)*Technological Institute of Patras*

Background: Treatment programs for children with ASD focus on early and intensive intervention reported to last usually two years. The question raised is what happens to these children beyond the intensive treatment period.

Objectives: The present report is on children with ASD who after an intensive treatment period for two years continued to be treated and followed up well into the primary school years. What was the outcome.

Methods:

Treatment program: It consists of three stage interventions provided at the Day Centre for Children with Developmental Disorders:

1. Intensive individual (behavior, speech, and occupation) therapy and family intervention. The individual sessions (4 to 6 per week) may last two years or longer depending on the case. The treatment objectives are set, by having first drawn a detailed assessment of the developmental profile of the child, and second by addressing the deficits with behavior methods (ABA and PRT).

2. Intensive socialization group therapy up to 12 hours a week for one year or longer. It consists of group work by two therapists with up to four

children, who may also continue receiving individual therapy sessions in selected areas e.g. speech-language therapy.

3. Attendance at regular kindergarten in the community while continuing a less intensive program at the Day Centre. Entry to primary public school follows. Older children who have successfully progressed through the previous stages continue with group therapy (including community outings) in the afternoon. Focused support and therapy continues well into the primary school years depending on needs. Children who do not develop adequate cognitive skills enter special schools (for the mentally retarded).

Subjects: Ten (10) children, out of 22 with ASD, completed the program (age 6-10) and are now attending regular public school classes. Their progress is examined. The child's growing ability to cope with the demands of a regular school environment was considered the criterion of substantial cognitive and psychosocial improvement. The school classroom teachers have been, with exceptions, not flexible dealing with our subjects, and some parents avoided even informing them on the developmental history of their child. The outcome was also assessed on a battery of tests and questionnaires (ADOS, ADIR, RAVEN, SDQ, VINELAND, PPVT-III, CELF-4, DELV, Academic Skills-Porpodas).

Results:

The outcome varied in behavior and cognitive abilities. The academic progress was adequate. Most children scored within the ADOS range. While most showed improved social behavior their pragmatic skills remained low.

Conclusions:

This ongoing project shows that children with ASD, despite great progress made which allowed them to attend regular school classes, might continue to present with some cognitive and behavior deficits which require continuing attention.

124.024 24 Outcome of Children with Autism and Intellectual Impairment Following an Intensive Treatment Program Including Edt. R. Blanc*, *INSERM U930*

Background:

Early diagnosis of autistic disorders has meant that young children with autism may be treated with several multidisciplinary and individualized therapies. However, understanding of the evolution is still incomplete as clinicians still have few appropriate evaluation tools that are sufficiently reliable for this complex developmental disorder.

Objectives:

This study reports the psychological and behavioural outcomes of a group of children with autism enrolled in an intensive treatment program including Exchange and Developmental Therapy, EDT. The aim of this study was to investigate the development of children with basic disorders of infantile autism such as impairment in social interactions and communication and resistance to change, using a new and complete assessment battery.

Methods: We selected 29 children, aged 2 to 8 years, with severe autism (DSM-IV T-R, APA, 2000, ADI-R, Le Couteur et al., 1989 and CARS, Childhood Autism Rating Scale, Schopler et al., 1986) and moderate to severe mental retardation (Brunet-Lézine scale-Revised, 1997 - French adaptation of Gesell scales, 1947). We examined cognitive and socio-emotional skills using a recently validated scale, the (SCEB) (Adrien, 2007 ; Thiébaud et al., 2010). Changes in autistic symptomatology were evaluated with the BSE scale (Behavioural Summarized Evaluation scale revised) (Barthélémy et al., 1997). The two types of assessment were performed at the beginning of treatment and then another developmental assessment was performed 10 months later, followed by behavioural evaluations every month. We compared clinical data at different times in the assessment process for each child

Results:

The results showed that this combined developmental and behavioral assessment could reveal not only general progress in cognitive and

socio-emotional skills but also decreases in autistic symptomatology. Progress was different from one child to another and seemed dependent on the initial severity of the mental retardation. Finally, although overall retardation did not change, significant reduction in autistic behaviours occurred with therapy.

Conclusions:

These results confirmed previous studies (Rogers, 1996; Schreibman, 1996; Adrien et al., 2002-b; Blanc et al., 2003; Howlin, 2005, Magiati, 2007 ; Wallace and Rogers, 2010) and indicated the value of this assessment battery which explores both the cognitive and socio-emotional development of the child and also follows the evolution of the autistic symptomatology. Moreover, this study identified functions sensitive and resistant to the intensive programme including Exchange and Developmental Therapy, EDT, indicating directions for prevention and early intervention.

124.025 25 Six-Months Clinical Outcomes Following Treatment As Usual (TAU) for Autism: Focus On Language and Communication. A. Narzisi*¹, F. Muratori² and .. IDIA Consortium³, (1)*University of Pisa - Stella Maris Scientific Institute*, (2)*University of Pisa – Stella Maris Scientific Institute*, (3)*Italian Health Services for Autism*

Background:

Language and communication impairments in children with autism spectrum disorders (ASD) are increasingly recognized. In 2011 Kjellmer showed that for children with ASD, receptive and expressive language is mainly related to cognitive level, whereas non-verbal communication skills seem to be also related to severity of autism symptoms and adaptive functioning.

Objectives:

To describe language and communication outcomes for ASD toddlers after six-months of treatment as usual.

Methods:

70 participants (57 males and 13 females; mean age = 35,2 months) with a DSM-IV-TR diagnosis for Autism or PDDNOS, confirmed by ADOS-G,

were recruited. Language and communication outcomes were studied using the following measures: ADOS-Communication; Griffiths-Language; Vineland-II scales (VABS); and MacArthur Communication Development Inventories (MCDI). Language/Communication measures were subdivided by cognitive level, measured using Griffiths Developmental Quotient (gr.1 IQ>70; gr.2 IQ 55-69; gr.3 IQ<55), and diagnostic group (Autism vs PDD-NOS) according to DSM-IV-TR. This study was funded by Italian Ministry of Health.

Results:

At baseline and at endpoint, cognitive level was related to the mean score such that gr.1 (IQ>70) showed the highest mean scores, the gr.2 (IQ 55-69) showed lower mean scores, and the gr.3 (IQ<55) showed the lowest. For the ADOS scores the trend was opposed. At six-months follow-up, in gr.1, improvements from T0 to T1 were found in: VABS Composite score ($p < .005$). In gr.2, improvements were found in: MCDI-Comprehension ($p < .005$); MCDI-Production ($p < .005$); MCDI-Gestures ($p < .005$); VABS-Communication ($p < .005$); VABS-Daily Living skills ($p < .005$). In gr. 3 improvements were found in: MCDI-Comprehension ($p < .005$); MCDI-Production ($p < .005$); MCDI-Gestures ($p < .005$); and ADOS-Communication ($p < .005$). Also, diagnoses were related to the mean score such that PDDNOS group showed the highest mean scores, and the Autism group showed the lowest. In Autism improvements from T0 to T1 were found in MCDI-Comprehension ($p < .001$); MCDI-Production ($p < .005$); MCDI-Gestures ($p < .001$); and ADOS-Communication ($p < .005$); VABS-Communication ($p < .005$); VABS-Daily Living skills ($p < .005$); and VABS-Composite ($p < .005$). In PDD-NOS improvements from T0 to T1 were found in: MCDI-Gestures ($p < .005$) and ADOS-Communication ($p < .005$).

Conclusions:

Our study showed two opposed findings. On the one hand, both at baseline than at endpoint, higher language and communication skills are mainly related to higher cognitive level and to lower severity of autism spectrum disorder; on the other side, at six-months follow-up, children with (a) severe/moderate developmental delay than

normal cognitive level; and with (b) less severe autism (PDDNOS than Autism) showed higher statistical and clinical outcomes. In conclusion, these findings highlighted the importance of considering these aspects when managing the early intervention and showed that treatment as usual seem to have played a role in having improved the Language/Communication skills especially in children with autism and moderate/severe development delay.

124.026 26 A Longitudinal Study On Teacch Program in Preschool Children with Autism Spectrum Disorder. L. D'Elia^{*1}, G. Valeri², S. Vicari¹, F. Sonnino¹ and A. Mammone³,
(1)Paediatric Hospital Bambino Gesù, (2)Children's Hospital Bambino Gesù, (3)Paeditric Hospital Bambino Gesù

Background: The TEACCH program is an educational intervention based on the collaboration between parents and professionals, aiming to promote personal independence, social responsibility and generalization of the child's skills in different setting (home and school), involving parents and teachers as co-therapist. Teaching parents is crucial to improve the generalization and maintenance of treatment gains over time, and therefore the inclusion of parents as treatment providers for their own children is now considered an essential component of autism intervention. Moreover, since the TEACCH method includes a home program intervention, it would be interesting to know if this method also reduces parental stress and consequently their perception of children's maladaptive behaviours. Several previous studies supported the effectiveness of the TEACCH program, conducted at home and school with different intensity, with positive developmental outcomes for ASDs children in natural environments.

Objectives: Our aim was to evaluate the effects of TEACCH program (at home and school) in ASDs preschool children, on autism severity, adaptive functioning, language skills, children's maladaptive behaviours and parental stress, compared to control group following a non-specific approach.

Methods: 15 subjects in the TEACCH group compared to 15 children receiving usual intervention and assessed for 4 times. Multiple measures of outcomes were used to address autism severity and behavioral profile.

Results: Both groups improved over time for autism severity, adaptive functioning, language skills, behavioral problems and parental stress. Significant changes were observed on ADOS classification from T0 to T3. The TEACCH group were decreased in Withdrawal, Problems in Pervasive Developmental and Attention deficit/hyperactivity, Internalizing and Total problems in CBCL subscales. Significant improvement were observed on "Parent-child difficult interaction" subscales of PSI-SF Questionnaire.

Conclusions: Findings suggest that a low intensity home and school TEACCH program may provide benefits to children with ASD, decreasing of autistic symptoms and/or reducing maladaptive behaviors. Furthermore a decrease of parental stress witness that an involvement of parents in the rehabilitation program is a crucial point that greatly contributes to treatment efficacy.

124.027 27 Comparing Applied Behaviour Analysis and Ipad Autism Applications; Early Social Skills Interventions for Young Children with Low Functioning Autism. J. R. Solomon*, *University of Western Sydney*

Background: Despite the rising prevalence and earlier identification of autism spectrum disorders (ASD), comparative research concerning early intervention is lacking. Further research is needed to establish best treatment practices that address social skills, a core deficit of autism, particularly for young children with Low Functioning Autism (LFA). The efficacy of Applied Behaviour Analysis (ABA) for young children with ASD requires further investigation (Boyd, Odom, Humphreys, & Sam, 2010). Moreover, emerging interventions, such as iPad Autism Applications (APPS), are being developed and put forward as an alternative to ABA. However, to date, there has been no experimental examination of the efficacy of APPS relative to ABA.

Objectives: This pilot study addresses this gap in the early intervention literature by evaluating the utility of APPS relative to ABA for improving social skills in young children with LFA.

Methods: An alternating treatments design with a multiple baseline served to evaluate ABA and APPS interventions across twelve participants, ages 2 to 6 ($M = 3.6$), on four social skills: eye contact, smiling, functional play and helping

others. All participants completed a four-week training program and received ABA for two social skills and APPS intervention for the alternate two social skills. A free-choice paradigm was employed to measure intrinsic motivation to interact with the respective interventions.

Results: A one-way repeated-measures ANOVA revealed significant improvements for both APPS and ABA interventions on eye contact measures, $F(3, 30) = 9.47, p < .001, \eta^2 = .49$, smiling measures, $F(3, 30) = 5.83, p < .05, \eta^2 = .37$, helping behaviour, $F(3, 30) = 17.42, p < .001, \eta^2 = .63$, and functional play, $F(3, 30) = 24.17, p < .001, \eta^2 = .71$. Independent t-tests demonstrated that interventions did not differ significantly with respect to skill acquisition and skill maintenance. No significant difference was observed between skill transfer from APPS to face-to-face social interaction and ABA skill maintenance. However, paired dependent samples t-tests showed skill transfer from APPS to face-to-face social interaction to be significantly greater than baseline level for eye contact, $t(5) = 3.44, p < .05$, helping behaviour, $t(5) = 4.56, p < .05$ and functional play, $t(5) = 5.05, p < .05$. A binomial test revealed APPS to be significantly more intrinsically motivating for participants than ABA, $p = .039$.

Conclusions: This study offers the first test of the efficacy of APPS for improving the social skills of young children with LFA. Taken together, the findings that APPS assisted with improving social skills and were intrinsically motivating to participants opens the door to interesting and exciting possibilities for the future of early intervention. The paper argues that, as there is no existing treatment that completely addresses the needs of children with ASD, a combination of eclectic, evidence-based strategies is advisable. Given the necessity of interacting with others for improving social skills, it is recommended that future investigations consider incorporating APPS into early intervention as an augmentative tool, rather than an alternative therapy.

124.028 28 Peer-Mediated Intervention in Young Children with Autism: Stay, Play, Talk. A. B. Barber*¹, R. W. Saffo², L. D. Craft² and H. Goldstein³, (1)*University of Alabama - ASD Clinic*, (2)*University of Alabama*, (3)*The Ohio State University*

Background:

The earlier intervention begins for children with autism, the more likely the intervention will guide brain and behavior development back toward a typical pathway (Dawson, 2008), and the more likely children will be included in regular education placements (Harris & Handleman, 2000). However, the efficacy of social communication interventions remains unclear (Rogers & Wallace, 2011). Recent evidence suggests that peer-mediated interventions (PMI) improve social communication skills of preschool and school-age children with autism (Chan et al., 2009; Goldstein et al., 1997, 2007). However, PMIs have not been implemented with children identified with autism in early childhood.

Objectives:

The purpose of this study was to examine the efficacy of the *Stay, Play, Talk* PMI (Goldstein et al., 1997) on the social communication of children with autism under age 4.

Methods:

Four intervention dyads were created; each included a child with autism (target child) and one typically developing preschooler (peer buddy). Pairs were matched on gender, socioeconomic level, and interests. Adapted from English et al. (1997), the interventionist taught the peer buddy to *Stay, Play, and Talk* across three 15-minute pre-intervention training sessions. Peer buddies implemented the *Stay, Play, Talk* strategies with their matched target child during two weekly 20-minute sessions across 16 weeks. Each target child's social communication acts were coded then analyzed across three types: uncoordinated gestures, coordinated gestures, and words with or without gesture. A total communication score (TCS) was created by combining initiation and response data for each participant. The investigators also coded the frequency and type of adult prompting required for the dyads to maintain engagement. Finally, the frequency of social communication acts per child-initiated topic was analyzed to determine which materials or activities were most likely to encourage balanced social communication turns among the target child and his peer buddy. The Early Communication Indicator (Greenwood, et al., 2006) was used to measure social language use

during a 5-min. individual play sample, pre- and post-the intervention phase).

Results:

A multiple baseline design across participants was implemented. Preliminary results are based on the TCS and the frequency of initiations and responses across 6-10 baseline sessions and 8 intervention sessions. Thus far, each child demonstrated stable baselines and a striking increase in TCS at the onset of intervention. Frequency of initiations and responses also increased above baseline data following the onset of intervention. Initiation and response data mirrored the pattern observed for TCS. However, the target children responded to the social communication of their peers more often than initiating it. This pattern fits the social communication profile for children with autism. Type of communication and frequency of adult prompting will also be presented. Video samples highlight the remarkable increase in social communication, as well as the relationships that developed among the peers.

Conclusions:

When used to supplement comprehensive early interventions, peer-mediated interventions show promise in the improvement of social communication in early autism for these children. Results of this study offer valuable clinical implications for the integration of peer-mediated intervention into daycares, homes, and other natural environments.

124.029 29 Language Development in Preschoolers with ASD: A Comparison of Outcomes Across Educational Settings. J. Atick*¹, C. S. Ghilain¹, A. Gutierrez² and M. Alessandri¹,
(1)University of Miami, (2)Florida International University

Background: Impairments in language in children with ASD are of particular interest to researchers because these skills have been shown to be strong predictors of overall ASD outcomes (Sztmari, Bryson, Boyle, Streiner, & Duku, 2003). When considering language development in the school environment, little is known about the difference in language gains between self-contained and inclusive preschool classrooms (Harris, Handleman, Kristoff, Bass & Gordon, 1990).

Objectives: This study seeks to determine the differences in language gains between self-contained and inclusive classrooms across a school year in preschool children with ASD.

Methods: This study is an extension of a larger, multi-site study comparing the efficacy of preschool educational programs for children with ASD. Children were administered the Preschool Language Scale, Fourth Edition (PLS-4) in order to measure their language functioning at both the beginning (PRE) and end (POST) of the school year. The data collected from this study were used to create language gain scores for Auditory Comprehension, Expressive Communication, and Total Language across educational settings (i.e. self-contained and inclusive preschool classrooms).

Results: No significant differences in language gains were found between the two classroom types on Auditory Comprehension ($t(184) = -.645, p = .513$). However, in terms of Expressive Language, a significant difference in language gains was found ($t(186) = -2.295, p = .027$) when comparing self-contained versus inclusive classroom. Total Language gains were also statistically significantly different across classroom type ($t(186) = -.645, p = .035$).

Conclusions: Average differences of children's language gains between self-contained versus inclusive classrooms were demonstrated in Expressive Communication and Total Language from the beginning of the school year to the end, with children in inclusive classrooms demonstrating greater language gains. Although language gains were made in all classrooms, it is important for future research to identify specific classroom characteristics (e.g., student:teacher ratios; ratio of typically-developing students to students with ASD; etc.) that promote increased gains in child language development.

124.030 30 Playing At Preschool: Engineering Playtime to Address Core Deficits. Y. C. Chang^{*1}, S. Patterson¹ and C. Kasari², (1)University of California, Los Angeles, (2)University of California Los Angeles

Background: Playing in preschool is often what children do best. However, for children with ASD play takes on special challenges as children are often rigid and impoverished in their play skills. While a number of studies have taught play skills

to children with ASD, these have often been carried out in 1:1 adult child therapy sessions, and may be less transportable to public preschool programs where teachers typically work with children in dyads or triads of children. To ensure that evidence based interventions are implemented and sustained in public preschools, alternative models are needed.

Objectives: To determine if a modified efficacious therapeutic approach (JASPER, Kasari et al, 2010) adjusted for small group instruction has a) sustainability and implementation by teachers in low resourced public preschool programs, b) teachers better able to identify targets of treatment and implement JASPER will have children who make greater change in play skills.

Methods: In collaboration with administration staff in a large school district, a preschool deployment model is currently being executed in all six specialized autism preschool programs in the district. Each program has two classes, an AM and PM class of 6-8 children each ($n = 57$). All preschools contain 80-100% of children on free and reduced lunch, and 91% ethnic minority. A randomized wait list control design is underway. Teachers (2 at each site) have been trained to assess all of their children with a modified brief play assessment that yields intervention targets of specific play skills. Targets chosen by teachers are validated against research assessments (by research team). Teachers in immediate treatment group are taught JASPER modified for group sessions in a coaching and consultation model with fidelity of implementation checks weekly. Teacher fidelity, match in intervention targets, and child change on play will be compared at end of 8 week treatment phase, and 4 week follow up phase to teachers who have learned to assess children in their classrooms but not taught the treatment.

Results: Thus far, all teachers have been taught the assessment, assessed their children and chosen treatment targets. Intervention consultation and coaching is underway for the immediate treatment groups. All data will be completed by February and children reassessed.

Conclusions: The results of this study will provide evidence of whether teachers who are more actively involved in the development, and

execution of the intervention (and assessment process) will have children who perform better on outcome measures.

124.031 31 Translating a Social Communication Intervention for Use in Authentic Education Settings. R. Landa*, *Kennedy Krieger Institute*

Background:

There is an urgent need to translate efficacious lab-based interventions into feasible, scalable, effective interventions for implementation in public preschool settings for children with ASD. School-based implementation of interventions targeting core social and communication ASD deficits could lead to significantly improved child outcomes and reductions in long-term special education costs for students with ASD. The 'Early Achievements' (EA) intervention was designed to improve interpersonal synchrony and communication functioning in toddlers with ASD and was shown to be effective within an RCT (Landa et al., 2011). Treatment gains were sustained through a 6-month post-intervention follow-up period. We have begun the first year of a three-year process of translating the EA intervention for implementation in public schools.

Objectives:

To define:

- (1) barriers to feasible implementation of an adaptation of EA into authentic educational settings for preschoolers and pre-kindergarteners with ASD;
- (2) iterative intervention and professional training development processes aimed at improving feasibility of implementation;
- (3) changes in teachers' fidelity of implementation of the adapted EA intervention and self-efficacy during the school year; and
- (4) changes in children's social and language performance from pre- to post-implementation of the adapted EA intervention.

Methods:

(1) Based on themes extracted from focus groups and classroom observations, barriers to implementation of the intervention were defined.

(2) Using our objective evaluation system, focus group and advisory committee members identified whether revisions to the original EA intervention surmounted the barriers defined in #1.

(3) Six teachers were trained to implement the intervention. Teachers were assessed prior to training, then monthly through the school year (dependent variables: self-efficacy and intervention fidelity scores).

(4) Seventeen children with ASD (mean age was 4 years at study start). Children were assessed prior to teacher training, then monthly through the school year (dependent variables: Mullen Scales of Early Learning Receptive and Expressive Language age-equivalents; frequency of initiation of joint attention and spontaneous imitation).

Results:

(1, 2) Specific strategic design elements in the intervention addressed barriers to feasible implementation such as: methods of linking the new supplemental interpersonal synchrony and language curricula to existing school curricula; teacher training design and timing (aided by video examples, planning guides, and self-evaluation guides); developing needed instructional materials; and developing the needed training for school administrators.

(3) Teachers' self-efficacy at pre-training ranged from 45-88%; fidelity ranged from 45-67%. (3, 4) Data acquisition is in process. Results to be obtained by, and presented at, IMFAR include changes, from the beginning of the school year (prior to teacher training) to school-year-end, in: teachers' self-efficacy and fidelity with increasing implementation experience; and children's performance per changes in the dependent variables listed above.

Conclusions:

There is a major gap between existing pre-professional teacher training and ASD students'

learning needs. Translating lab-based efficacious interventions for use in the public sector has challenges that are surmountable. Data obtained by IMFAR will reveal, preliminarily, whether our iterative translation process was associated with improvement in teachers' self-efficacy and fidelity, and whether children in classrooms of trained teachers gained in interpersonal synchrony and language skills.

124.032 32 Evaluating the Effectiveness of Early Interventions On Social Communication Outcomes for Young Children with Autism. J. D. Bryant*, L. H. Hampton, M. Y. Roberts and A. P. Kaiser, *Vanderbilt University*

Background: Deficits in social communication are a core feature of autism and are apparent in children with autism as early as their second year (Adamson, Bakeman, Deckner, & Ronski, 2009; American Psychiatric Association, 1994; Weismer, Lord, & Esler, 2010). For over a decade, early intervention has been recommended as a way to address deficits (National Research Council, 2001; Lord & Bishop, 2010). A range of interventions targeting communication and other developmental outcomes have been developed and researched. However, the effectiveness of these early interventions in increasing expressive language has not been reviewed systematically.

Objectives: The purpose of this study was to review the features of early interventions addressing communication skills and examine the magnitude and range of effects of these interventions on expressive language outcomes for young children with autism.

Methods: Nine high quality group experimental studies addressing communication outcomes for young children with autism were included in this study. Study inclusion criteria included: (1) group design experimental studies, (2) included at least one intervention that addressed social communication skills, (3) measured one or more expressive language outcomes, (4) participants diagnosed with or at risk for autism, (5) participants with a mean age less than or equal to 42 months, (6) published in peer reviewed journals, (7) written in English, and (8) published between 1985 and 2012. Studies were selected through a keyword search of online databases and archival searches; then, abstracts were screened for key components. Studies meeting criteria were coded for: child characteristics (IQ, severity, age),

the type of intervention approach (developmental, behavioral, or hybrid), agent of intervention, extent of parent involvement in intervention, the intensity and duration of treatment, and child social communication outcomes. Effect sizes were calculated for expressive language outcome measures.

Results: Although all nine studies assessed communication outcomes, studies varied widely in the extent to which they explicitly targeted social communication and the measures of social communication. A total of 480 children with autism participated in these studies, ranging in age from 12 to 54 months at the start of the studies. Fifty-six percent of these interventions were developmental in approach, 11% were behavioral, and 33% were hybrid. Length of interventions ranged from 3 to 24 months. All studies included a parent-training component. Effect sizes for expressive language varied across studies, ranging from .06 to .58. Four studies used the MacArthur-Bates Communicative Development Inventory (*MCDI*; $d = 0.38-0.58$), three used the Mullen Scales of Early Learning-Expressive Language subscale (*MSEL*; $d = 0.06-0.56$), one used the Early One-Word Picture Vocabulary Test (*EOWPVT*; $d = 0.18$), and one used the Communication and Symbolic Behavior Scales (*CSBS*; $d = 0.43$).

Conclusions: Although all interventions targeted social communication, expressive language outcomes varied by intervention and measure. Across studies there was evidence that early intervention did improve expressive language. Additional analyses are needed to examine the intervention features associated with differential outcomes and child characteristics that predict expressive language outcomes.

124.033 33 Promoting Social Responsive Between Primary Caregivers and Children with Autism. E. (. M. Maher*, *University of Sydney*

Background:

Difficulties in the development of the capacity and desire to reference others, communicate to share subjective experiences and establish joint attention are core characteristics of autism. Evident in very young children with autism, these deficits have profound effects on the development of cognition, communication and social relating.

Objectives:

This study involved implementation of a caregiver training program conducted over a 6-month period, derived from a developmental social pragmatic orientation, and using the Relationship Development Intervention (RDI) Program model (Gutstein, 2009). The goal was to determine whether an increase in adult-initiated declarative bids were more successful at facilitating experience-sharing and child responsiveness than bids that were imperative in nature.

The study examined the effects of instructing caregivers to use specific communication strategies and the impact of the overall use of such strategies on children's communication outcomes and general functioning. The research set out to examine verbal and nonverbal communication bids by caregivers when interacting with children with autism. The aim was to determine whether bids that were declarative were more successful at facilitating rate of child responding during interactions, compared to imperative bids for communication. As well as determining the rate of responding, the quality of the child response (responsiveness) was also determined as measured through experience sharing responses.

Methods:

A nonequivalent groups quasi-experimental design, with two experimental and one comparison (control) group with pre-test and post-test measures, was used to demonstrate the feasibility of implementing a relationship-focused model, with detailed documentation of group treatment effects and individual results. Analyses of changes in pre and post-test measures were conducted for children and caregivers. A total of 16 children on the autism spectrum, aged between 3.9 and 8 years were involved in the project. The study examined the effects of instructing caregivers to communicate to invite experience-sharing by increasing their frequency of declarative communication initiations. A comparison group received the usual program provided at the centre. The ratios of imperative to declarative communication bids of the care-givers were measured pre and post intervention, as were child social responsiveness, communication

skills, adaptive functioning and measures of parental stress and coping.

Results:

Descriptive statistics were used to present the results where outcome measures were analysed to measure change and to assess the benefits of the intervention. Findings suggest that parents and staff were able to successfully modify their communication in the desired declarative manner, as evidenced by video-recorded play sessions. Furthermore, adult communicative adaptation appeared to correspond with increased child responsiveness. Other measures conducted at post-test, showed variable results, supporting the need for larger, controlled, longitudinal studies.

Conclusions:

Promoting positive caregiver and child interactions, and the implications of such exchanges, provide valuable insights. There is a compelling argument for consideration of the impact of adult communication and interactional style on the ability to influence the types of communicative functions used by children with autism. If caregivers are taught to adapt their communication style with the child with autism so that they use more declarative communication, they are likely to facilitate aspects of social-communicative development.

124.034 34 Differential Effects of Video Modeling As a Function of Targeted Social Behavior for Children with Autism. J. B. Plavnick*, M. C. MacFarland, S. J. Ferreri and S. Hur, *Michigan State University*

Background: Video modeling is a commonly used instructional procedure and is now established as an evidence-based practice for teaching individuals with autism (Mason et al., 2012). The procedure involves showing a video display of a model performing a target behavior to an observer and then providing an opportunity for the observer to perform a similar skill. Despite an abundance of recent research examining video modeling for children with autism, several questions remain regarding the efficacy of the procedure when applied to various skills. Additionally, minimal research has examined the possibility of leveraging the attention-capturing qualities of video to simultaneously teach multiple

students with autism who would otherwise require one-to-one instruction in order to ensure the student attends to the instructional material.

Objectives: The primary objective of this study was to examine the effects of video modeling when applied to two types of social initiations: inviting peers to share in play and asking to join others in play. The effects of video modeling on physical and verbal behaviors associated with inviting to play and asking to join in play were compared for 3 children with autism. A secondary objective was to assess the feasibility and preliminary efficacy of video modeling when administered to a small group of preschool students with autism.

Methods: A single-case reversal design was used to examine the relation between video modeling and the acquisition of specific social initiations directed toward peers by three preschool boys diagnosed with autistic disorder. Two sets of videos of peer models demonstrating the target behaviors were recorded and displayed for all participants simultaneously using an Apple iPad. Participants were then given the opportunity to perform the modeled behaviors by interacting with their peers during a social skills group session.

Results: During a baseline condition that did not include video modeling, participants demonstrated minimal social initiations. When video modeling was introduced for inviting peers to play, participants imitated some physical initiations though results were variable across sessions. None of the participants engaged in verbal initiations during this condition. All participants showed higher levels of physical and vocal initiations directed toward peers when video modeling was applied to asking to join in play.

Conclusions: The outcomes of the present investigation support previous research suggesting that video modeling can have differential effects based on skills targeted. The results also suggest video modeling, when used for certain social behaviors, has potential as a methodology for teaching young children with autism in small group settings. These results have implications for the selection of social targets when using video modeling and may offer considerations about procedural elements of the intervention. Future research that examines how

video modeling alters behavior is needed to better understand the target behavior selection process and procedural components ideal for an individual student.

124.035 35 Coordinated Positive Engagement During Social Interactions in Infancy: An Early Identification and Intervention Study. J. Bradshaw*, A. Navab, S. Lucyga, L. K. Koegel and R. L. Koegel, *University of California, Santa Barbara*

Background:

Recent findings that earlier intervention results in greater gains for infants and toddlers with autism spectrum disorder (ASD; Rogers, et al. 2012) necessitate ascertainment of early, reliable ASD indicators. However, ASD behavioral risk factors in infants under 12 months of age remain difficult to identify (see Zwaigenbaum, 2010). One leading hypothesized risk factor for autism in the first year of life has been social attention during play with objects, i.e. joint attention and joint engagement (Adamson, et al. 2012; Mundy, et al. 2009). Little is known, however, about social attention in young at-risk infants during face-to-face dyadic interactions (i.e. without objects). This type of paradigm allows for analysis of pure social attention in which the focus of the interaction is not an object, but rather the caregiver. Moreover, few studies have investigated a) differentiating characteristics in six-month-old infants already exhibiting concerning social behaviors nor b) early intervention focused on improving social attention.

Objectives:

The current study investigates early patterns of social attention in face-to-face dyadic interactions through repeated measures of infants exhibiting significant concern for ASD (high-concern) and typically developing infants (no-concern). A social intervention treatment is additionally explored as a method of improving social attention in high-concern infants.

Methods:

Seven six-month-old infants participated in this study. Infants first participated in a social assessment, which determined their assignment to the "high-concern" or "no-concern" participant

group. Four infants exhibited high concern for social difficulties and three exhibited no concern for social difficulties based on parent report and clinical assessment. High-concern infants participated in a systematic time-series analysis of baseline followed by an intervention designed to improve social engagement. During assessment and intervention phases, each infant-caregiver dyad participated in multiple measures of face-to-face interaction. These interactions were videotaped and coded for infant behaviors: affect, social interest, gaze to face of caregiver, positive engagement (positive affect and gaze to face), and neutral engagement (neutral affect and gaze to face).

Results:

During the initial assessment phase, high-concern infants showed notably less social interest and lower positive affect during play scenarios than the no-concern infants. Additionally, when looking at the face, they exhibited lower levels of positive engagement and higher levels of neutral engagement.

Following a social engagement-based intervention, high-concern infants' attention patterns showed more overall positive affect and social interest during face-to-face interactions. They additionally slightly increased positive engagement while markedly decreasing neutral engagement during interactions. Attention patterns after intervention paralleled no-concern infants' social attention patterns.

Conclusions:

Despite challenges identifying behavioral markers in six-month-old infants, the present study provides preliminary evidence that an assessment incorporating high-concern and no-concern infants may elucidate differentiating characteristics related to social engagement. The addition of an experimental paradigm in which parent-infant dyads are assessed during face-to-face play may provide new insight in regard to early diagnosis markers. Specifically, this research identifies differences in affect associated with social attention, rather than solely visual scanning. Lastly, this intervention markedly improved social attention of high-concern infants to increasingly

mirror the no-concern infants, suggesting feasibility of developing social interventions for high-risk infants.

Core Deficits Program

125 Core Deficits: Social Understanding

125.036 36 Psychometrics of the Chinese Mandarin Version of the Social Responsiveness Scale (SRS) in a Taiwanese Population of Children Aged 6-8 Years. C. L. Chang*¹, L. C. Lee², P. C. Tsai², R. Harrington², I. T. Li³ and F. W. Lung⁴, (1)*Kaohsiung Armed Forces General Hospital*, (2)*Johns Hopkins Bloomberg School of Public Health*, (3)*Calo Hospital*, (4)*Taipei City Hospital*

Background: Autism Spectrum Disorders (ASDs) represent one end of a larger spectrum of quantitative impairment that is continuously distributed in the general population. The Social Responsiveness Scale (SRS) is an instrument that characterizes quantitative impairments in social awareness, cognition, communication, motivation, and repetitive behavior/restricted interests that define ASD, and provides a more subtle characterization of individual symptoms than using traditional classification systems. Reliability and validity of the tool need to be established before its adaption in non-Western populations.

Objectives: To report reliabilities and validities of the Chinese Mandarin Version of the SRS in a large population of school children aged 6-8-years, and in children who are at high risk for ASD.

Methods: Caregiver-reported SRS data were collected by an epidemiologic autism study recently conducted in PingTung, Taiwan. Raw scores of the total SRS and five subscales (social awareness, social cognition, social communication, social motivation, and autistic mannerisms) were used for this analysis. As recommended in the literature, a raw score of ≥ 70 in males and ≥ 65 in females is a cut-point that provides evidence for the presence of an ASD. Based on these cut-points, we defined the clinical (high risk for ASD) vs. non-clinical groups separately for males and females. Reliability was assessed using alpha, while validity was examined by factor analyses. Both reliability and validity analyses were carried out in the clinical group (high risk for ASD) and the full study sample (clinical and non-clinical combined).

Results: Because SRS score is sex specific, only data from participants who completed the SRS and whose child's sex is known are included in the analysis: 1384 males and 1507 females. Of those, 357 children (172 males and 185 females) met the recommended clinical cut-off and are classified as the clinical group. Reliability Alphas for SRS full scale, social awareness, social cognition, social communication, social motivation, and autistic mannerisms are 0.94, 0.54, 0.74, 0.85, 0.69, and 0.87, respectively, in full study sample (n=2891); and are 0.83, 0.10, 0.25, 0.64, 0.43, and 0.79, respectively, in the clinical group. Results from exploratory factor analysis showed factors loaded differently between the clinical group and the full study sample.

Conclusions: Reliabilities of the SRS full scale in both the full study sample and the clinical group are excellent and good. However, reliabilities of the subscales are overall poor in the clinical group, even given the sufficient sample size (n=357). Possible explanation on the different loaded factors for the full study sample and the clinical group will be further discussed.

125.037 37 Observation, Parent, and Self Report of Social Engagement in Adolescents with ASD. K. M. Burner*¹, F. Orlich², R. Oti², R. Montague², R. Poole², R. Bernier¹, B. H. King³, C. Lord⁴ and C. Kasari⁵, (1)University of Washington, (2)Seattle Children's Research Institute, (3)University of Washington and Seattle Children's Hospital, (4>Weill Cornell Medical College, (5)University of California Los Angeles

Background: Individuals with ASD often exhibit limited insight into their peer relationships. As a result, parent report is frequently utilized in ratings of youth social engagement. In fact, individuals with ASD display a systematic tendency to over-rate their social functioning relative to parents' report (Lerner et al., 2012; Vickerstaff et al., 2007). These informant discrepancies suggest the need to include observer measures of social functioning, particularly when examining change in social functioning in response to intervention. Unfortunately, there is limited research examining convergence among observation, parent, and self report in ASD.

Objectives: The main objective was to examine the relationship between observation of teen engagement and adolescent and parent report of

engagement and social interactions during a school-based social skills intervention.

Methods: Adolescents with ASD (n = 34) participated in an 8-week social skills intervention in the school setting. The Teen Observation of Peer Interaction (TOPI) was administered during school lunches at pre-intervention and post-intervention. The Teen Observation of Peer Interaction (TOPI) is a behavioral observation measure that allows for observation of peer interactions (e.g., proximity to peer, level of complexity in social engagement with another peer). The TOPI consists of five 90-second observation intervals and rates "engagement state" from "solitary" to "joint" on a six point scale for each interval. An overall average engagement state was calculated at each time point. In addition to completion of the TOPI at each time point, parent and self report measures of adolescent engagement and social interactions were collected via the Behavior Assessment System for Children (BASC) and Social Skills Improvement Scale (SSIS). Adolescents also completed the Index of Peer Relations (IPR).

Results: Adolescent report of engagement (SSIS), social stress (BASC), and interpersonal relatedness (IPR) were not related to engagement state (TOPI) at pre-intervention. However, at post-intervention, adolescents who were observed in more complex engagement states reported stronger peer relationships via the Index of Peer Relations ($r = -.509, p = .007$) (lower IPR = better peer relationships) and lower social stress via the BASC ($r = -.451, p = .012$). There continued to be no correlation between self-report of engagement on the SSIS and observation of engagement. Parent report of social engagement (SSIS) was significantly correlated with observation of engagement state (TOPI) at pre-intervention ($r = .535, p = .001$) and post-intervention ($r = .459, p = .024$).

Conclusions: Adolescents who were observed in more complex engagement states reported stronger peer relationships and lower social stress at post-intervention. Observer rating of adolescent engagement was convergent with parent, but not adolescent report of engagement at both time points. Although these relationships need to be explored further, these preliminary results suggest that there is validity in using observer report of

engagement in addition to self-report and parent-report when measuring impact of intervention on social engagement.

125.038 38 Being Imitated and Empathy for Pain in Adults with High Functioning Autism. J. R. Wiersema*, L. De Coster and M. Brass, *Ghent University*

Background: Imitation and empathy skills are thought to be impaired or delayed in adults with high functioning autism (HFA), and have theoretically been linked to dysfunctional shared representational mechanisms ('broken mirror' theory). However, more and more research on this theory shows conflicting results. In a recent study, we have related imitation literature and research on observing others in pain in typically developing adults. It was shown that being imitated enhances affective responding to seeing someone else in pain (empathy for pain), and we provided evidence for the role of shared representations in the sensory and the motor domain as a core underlying mechanism. If the shared representational system is important in understanding the problems of adults with HFA, it may be expected that the influence of being imitated on empathy for pain is different in this group compared to typically developing adults.

Objectives: To investigate the influence of being imitated on empathy for pain in adults with HFA compared to typically developing adults, and gain insight into the role of (dysfunctional) shared representational mechanisms.

Methods: We used startle eye blink data and skin conductance responses as indices of empathy for pain. Physiological data were obtained from 12 typically developing adults (mean age = 28 years, SD = 4.85) and 20 adults with HFA (mean age = 31 years, SD = 6.01). Startle blink and skin conductance responses were measured during presentation of a pain movie in which a hand on a screen received painful stimulation. Data were obtained in two conditions, in which 1) participants made finger movements which were imitated by the hand on the screen prior to watching the pain movie, or 2) participants made finger movements which were not imitated by the hand on the screen.

Results: Although still preliminary, results show that for both physiological measures, overall affective responses while watching the pain

movies were the same, if not higher, in adults with HFA compared to typically developing adults. However, results also suggest a three-way interaction between group, condition (imitation versus non-imitation), and half (first versus second half of the experiment). Typically developing adults showed higher empathy for pain after being imitated during the whole experiment, replicating previous studies. Adults with HFA, however, showed a reversal of the effect over time: while affective responding was lower after being imitated during the first half of the experiment, affective responding in the second half of the experiment was higher after being imitated (mimicking the pattern found in the group with typically developing adults).

Conclusions: In adults with HFA, the influence of being imitated on empathy for pain changes over time, with a reversed effect compared to typically developing adults in the beginning of the experiment and a similar effect at the end. Together with equal overall affective responding in both groups, these results suggest intact empathy for pain in adults with HFA and do not provide evidence for the 'broken mirror' hypothesis, but rather suggest dysfunctional control over these shared representational systems in adults with HFA.

Cognition and Behavior Program

126 Cognition and Behavior I: Sensory-Motor Processing

126.039 39 A Dynamic Approach to the Audiovisual Integration of Socio-Linguistic Information. M. Segers* and J. M. Bebko, *York University*

Background:

Individuals with ASD show deficits in the integration of audiovisual information, specifically in regard to temporal synchrony in speech (Bebko et al., 2006). Children with ASD perceive temporally discrepant audiovisual information as synchronous twice as often as typically developing (TD) children (Foss-Feig, et al., 2010). One way of measuring sensitivity to temporal synchrony is through the *temporal binding window* (TBW), the range of temporal offsets within which an individual perceptually binds inputs across modalities. Wider TBWs result in inadvertent associations between sights and sounds in the day-to-day environment, leading to chaotic representations of the world.

TBWs vary across experimental tasks and type of stimuli (e.g., speech, non-speech; Vroomen & Keetels, 2010). Common strategies to measure the TBW include synchrony judgment (SJ) tasks and temporal-order judgment (TOJ) tasks, both of which depend on passive cognitive judgments (i.e., dichotomous choice). In this study, a novel task was developed to elicit *active synchrony manipulation*, allowing participants to manually adjust the audio track of an audiovisual event in decisions regarding synchronicity.

Objectives:

Characterize audiovisual integration in TD adults and adults with ASD. Specific objectives:

- Explore the relationship between audiovisual integration and characteristics of ASD.
- Examine the temporal binding window using a novel, *participant-manipulated* task and compare to a standard *SJ* task.
- Determine how stimulus content influences the size and symmetry of the TBW.

Methods:

- Participants: Data for 30 TD adults have been collected and analyzed. Data collection for the ASD sample is partially complete and in progress.
- Stimuli:
 - Social Linguistic (SL), Non-Social Non-Linguistic (NSNL), and Social Non-Linguistic (SNL)
- Measures:
 - A *participant-manipulated*, audiovisual task allowing participants to manually adjust synchrony from a point of extreme audio delay or advance to a point of perceived synchrony.
 - A *synchrony judgment* task (yes-no) in which participants judge the synchronicity of video clips with

varying degrees of audio delay and advance.

- A combination of questionnaires (*Autism Spectrum Quotient*; *Empathy Quotient*; Baron-Cohen, et al., 2001), diagnostic reports, and diagnostic assessments (i.e., Autism Diagnostic Observation Schedule) to measure degree of autism-like traits in both samples.

Results:

1. *Temporal Binding*. Analyses revealed significantly larger TBWs in the *participant-manipulated* task compared to the *SJ* task with NL ($t=8.24, p<.001$) or SNL ($t=5.68, p<.001$) stimuli. However, for linguistic stimuli, no difference between tasks suggests relative stability in processing of speech information across tasks.
2. *Audiovisual integration and ASD*. Preliminary analyses in the ASD sample indicate larger TBWs across all three trial types (SL, SNL, NSNL) compared to TD participants.
3. *Autism traits and TBWs*. For TD participants, the AQ Social Skills subscale was correlated with TBW width for the linguistic ($r=.402, p=.03$) and social non-linguistic ($r=.458, p=.01$) conditions. ASD data are being analyzed.

Conclusions:

This novel task provides a new perspective on audiovisual integration by allowing individuals to actively *control* and *monitor* synchrony versus simple yes-no responding to experimenter-defined stimuli. Correlations between autistic traits and TBWs provide novel evidence that sensory-processing deficits contribute to core deficits including linguistic and social skills.

126.040 40 Assessing the Development of Visual Shape Perception in Autism: Influence of Local Information. A. Perreault^{*1}, C. Habak², L. Mottron³, F. Lepore⁴ and A. Bertone¹, (1)Perceptual Neuroscience Laboratory for Autism and Development (PNLab), (2)Centre de Recherche, Institut Universitaire de Gériatrie de Montréal, (3)Centre d'excellence en Troubles envahissants du développement de

Background: Studies investigating visual perception in autism have identified altered perception at early (local) and higher (global) levels of visual analysis. However, much less is known about whether alterations at each level are related, and if so, whether such relationships differ at different periods of development. To assess whether a local attribute differentially affects global shape perception in autism as a function of development, sensitivity to Radial Frequency Patterns (RFPs; Wilkinson et al 1998; Grinter et al 2010) was assessed. RFPs are closed-contour shapes whose local spatial characteristics can be manipulated by creating "bumps" or RFs along their quasi-circular contours. Depending on the number of bumps, both local and global processing strategies can be targeted. Moreover, RFPs are known to target intermediate (global) levels of analysis, which precedes object perception. Local RFP attributes can also be manipulated by changing the physical attributes (i.e. luminance vs texture) defining their global contour, a manipulation that targets early level visual processes.

Objectives: To assess whether the types of local information, mediated by early level perception, differentially affect intermediate level (global) visual perception in autism at different periods of development.

Methods: 40 autistic and 44 non-autistic participants, matched for full-scale IQ and age, were placed into school-aged (7-12 years), adolescent (13-17 years) and adult (18-27) age groups. All participants were asked to discriminate between perfect circles and RFPs, whose contours (a) contained either 3, 5, or 10 bumps or RFs, and (b) were either luminance- or texture-defined. The size (or amplitude) of the bumps was varied: the larger the amplitude, the easier it was to discriminate a RFP from a perfect circle. Participants were asked which of two successively presented stimuli contained the RFP (target); the other was a perfect circle. RFP discrimination thresholds were measured using a method of constant stimuli and a 2-ATFC procedure. All participants had to complete a total of 6 experimental conditions.

Results: Separate 2 (group) X 3 (age group) X 3 (# of RFs) mixed factorial ANOVAs were conducted for luminance- and texture-defined RFP conditions. For luminance-defined RFPs, no group-differences were identified at any RFP condition for any of the developmental periods assessed. For texture-defined RFPs, group-differences were identified for adolescents and adult groups, with decreased performance across both global (3 and 5 RFs) and local (10 RFs) RFP conditions in autism.

Conclusions: The differential effect of type of local attribute (luminance vs texture) on global shape discrimination supports the hypothesis that decreased global perception in autism, when present, may have early (local) visual origins. Specifically, manipulating the complexity (from luminance to texture) of local attributes affected global shape perception to a greater extent in autism. Since the perception of certain types of objects, such as faces, is believed to be preceded by global shape analysis, it can be argued, based on the present results that alterations at early levels of analysis can in part contribute to the atypical perception of objects in autism, and this is especially evident later in development.

126.041 41 Associations Between Autistic Traits, Sensory Processing Abnormalities and Anxiety Symptoms in Adults. J. Horder^{*1}, C. E. Wilson², M. A. Mendez³, D. De La Harpe Golden³ and D. G. Murphy⁴, (1)*Institute of Psychiatry, King's College London*, (2)*King's College, London*, (3)*King's College London*, (4)*Institute of Psychiatry, King's College London*

Background: Sensory processing abnormalities are increasingly recognized to be a key symptom of autism spectrum disorders (ASDs). Unusual sensory experiences, including both hypersensitivity and hyposensitivity, are hypothesized to underlie many of the characteristic features of ASDs, including repetitive behaviours and stereotypies such as 'stimming'. Previous studies have reported high rates of sensory features in individuals with an ASD, and recently studies in the general population have found that subclinical ASD traits are also correlated with reports of unusual sensory experiences, consistent with the broad ASD phenotype model. However, anxiety is also common in ASD and it has been suggested that anxiety mediates the association between ASD and altered sensory processing.

Objectives: We conducted the largest study to date of ASD traits, sensory experiences, and anxiety symptoms, in a sample consisting of adults both with and without an ASD, in order to discover whether ASD traits are associated with sensory symptoms, and to investigate whether anxiety is a mediating factor.

Methods: Participants (n=956) were recruited via online advertisements. Participants provided basic demographic details, details of their ASD diagnosis (if any), and completed the following self-report measures: the Autism Quotient (AQ), Adult/Adolescent Sensory Profile (AASP), Glasgow Sensory Questionnaire (GSQ), Cardiff Anomalous Perception Scale (CAPS), and Spielberger Trait Anxiety Inventory (STAI). Total scores were calculated, and Pearson's correlation coefficient was used to calculate bivariate correlations among scores.

Results: Consistent with previous reports, we found that reported sensory symptoms (AASP, GSQ and CAPS) were correlated with autism trait scores (AQ): AASP/AQ: $r=0.34$; GSQ/AQ: $r=0.49$; CAPS/AQ: $r=0.31$ (all $p's < 0.001$). Further, for the first time in adults, we show that anxiety is also correlated with both AQ scores and with sensory behaviours: STAI/AQ: $r=0.48$; STAI/AASP: $r=0.39$; STAI/GSQ: $r=0.41$; STAI/CAPS: $r=0.34$ (all $p's < 0.001$). These correlations remained significant when considering separately only the participants with and without a diagnosis of ASD. Also, we found that both sensory and anxiety symptoms were independently associated with AQ scores, even after covarying for the other (all $p's < 0.001$). Furthermore, we show that these results are not accounted for by gender, age, or presence of psychiatric comorbidity.

Conclusions: In adults, autistic traits are associated both with high levels of anxiety, and with sensory processing abnormalities. This was evident across the ASD spectrum and including general population neurotypical controls, confirming that these are important facets of the ASD phenotype. Our results suggest that both anxiety and sensory abnormalities are independently related to ASD, but also associated with each other. This suggests that in individuals with an ASD, abnormalities with sensory processing and anxiety symptoms are linked, but separate, phenomena. Implications for the

assessment and treatment of ASD will be discussed.

126.043 43 Cognitive and Behavioural Comorbidity of Social and Motor Difficulties in Primary School Age Children. L. Kenny*¹, E. L. Hill² and A. Hamilton¹, (1)University of Nottingham, (2)Goldsmiths University

Background: There is substantial comorbidity between different developmental disorders. For example, 50-80% of children with autism spectrum condition also have motor control difficulties (Green et al., 2009), and children with developmental coordination disorder may also struggle with social skills. Research on cognitive processes in developmental disorders has typically examined one disorder at a time without regard to comorbidity. Thus, the cognitive difficulties causing particular patterns of comorbidity remain largely unknown.

Objectives: This project aims to define the relationship between motor and social difficulties in children and the cognitive processes underlying these behaviours, in order to understand comorbidity in developmental disorders. We have selected three cognitive systems to investigate: 1) theory of mind systems, 2) mirroring systems and 3) systems of motor control. The present study aims to examine the relationship between these three cognitive systems and social and motor behaviour, across a large population of children with and without developmental disorders.

Methods: Social and motor behaviour were assessed by parent questionnaire (Social Responsiveness Scale (SRS); Developmental Coordination Disorder Questionnaire (DCDQ); and Conners 3 ADHD Index) in a sample of 142 children aged between 5 and 11 years old. A subset (n=68 so far) of these children completed detailed cognitive testing (Raven's matrices, theory of mind tests, action comprehension tests and motor control tests). Regression analyses were used to determine how well social behaviour (SRS scores) could be predicted based on the different cognitive test scores.

Results: A linear regression on the parent questionnaire data (n=142) found that scores on the DCDQ ($t(139)=-5.44$, $p=.000$) and the Conners 3 ADHD Index ($t(139)=5.61$, $p=.000$) significantly predicted scores on the SRS while age was not a significant predictor ($t(139)=1.66$,

$p=.099$). A preliminary linear regression on the results from the cognitive test battery ($n=68$) revealed that SRS scores were significantly predicted by performance on motor planning, motor sequencing and posture knowledge tasks, but not by theory of mind scores or non-verbal IQ.

Conclusions: The present study confirms previous reports of substantial overlap between parental reports of motor, social and attentional behaviours. More critically, we show that performance on lab-based motor tasks predicts a child's SRS score. Further analyses of this rich dataset will reveal the ways in which certain cognitive systems relate to the behavioural profiles that form the basis for diagnosis of developmental disorders such as ASC and DCD.

126.044 44 Deficit in Auditory Sensory Memory in Adults with High Functioning Autism. M. Erviti*¹, L. Demany¹, M. Bouvard¹, C. Galéra², A. Amestoy² and C. Semal¹, (1)*Université de Bordeaux*, (2)*CH Charles Perrens*

Background:

Many studies have shown that autism is associated with atypical perceptual functioning, in vision as well as in audition. In the field of audition, these perceptual particularities include a hypo- or hyper-sensitivity to certain sounds, and also sensory capacities above average. It seems well established that the perception of simple sounds (pitch discrimination and categorization of pure tones) is finer in individuals with high functioning autism (HFA) than in typically developing (TD) persons. For more complex sounds, there is no consensus: some authors have claimed that temporal processing is altered while others failed to find differences between individuals with HFA and TD persons. Auditory sensory memory has been given less attention in the literature, but one study employing simple sounds suggests that it may be overdeveloped in individuals with HFA. To our knowledge, there are no studies on the sensory memory of complex sounds in autism.

Objectives:

The aim of this study is to determine if adults with HFA differ from TD adults with respect to the perception and memory of meaningless and physically complex auditory stimuli, consisting of

wideband noise. Preliminary results are presented here.

Methods:

The study currently includes 10 participants with HFA and 14 TD persons. The chronological ages range from 16 to 28 years for the participants with HFA, and from 18 to 27 years for the TD individuals. Two tasks are proposed to the participants.

In the "Perception" task, one has to detect, within white noise acting as a masker, a signal consisting of a repeating, brief segment of white noise (varied from trial to trial). The independent variable is the signal-to-masker (S/M) intensity ratio. An adaptive procedure is used to measure the S/M ratio for which the signal is just detectable.

In the "Memory" task, one has to judge whether a noise (varied from trial to trial) is periodic or not. An adaptive procedure similar to that employed in the Perception task is used to measure the longest period for which periodicity is still detectable.

Results:

In the Perception task, our current results show no significant difference in performance between participants with HFA and TD persons. In the Memory task, by contrast, performance is significantly worse in the participants with HFA than in the TD participants.

Conclusions:

Our study suggests that autism has a stronger impact on auditory sensory memory than on auditory perception. However, further investigations are needed to clarify the characteristics of auditory memory in autism. We used here acoustic stimuli which were very complex both spectrally and temporally. Simpler stimuli and different tasks will have to be employed in the subsequent studies.

126.045 45 Elevated Motion Coherence Thresholds for Slow Stimuli in Individuals with Autism. C. Manning*¹, T. Charman², D. Aagten-Murphy³ and E. Pellicano¹, (1)*Centre for Research in*

Background: While some studies have reported elevated motion coherence thresholds in autism, others report motion coherence thresholds comparable to those of typically developing individuals. This discrepancy may, at least in part, be attributable to differences in task and stimulus parameters across studies. Some authors have suggested that individuals with autism process speed information differently to typically developing individuals. Such atypicalities in speed processing may therefore have an effect on coherent motion perception.

Objectives: We sought to investigate whether the speed of coherent motion was a contributing factor in determining the extent of differences between autistic and typically developing individuals.

Methods: We measured motion coherence thresholds under slow (1.5 deg/sec) and fast (6 deg/sec) speed conditions in children with an autism spectrum condition aged 7 to 14 years (n = 23), and age- and ability-matched typically developing children (n = 25). Stimuli were pairs of limited lifetime random dot stimuli presented sequentially: one stimulus had dots moving in random directions, and one stimulus had a proportion of dots moving coherently leftwards or rightwards. Participants were asked to select the interval containing coherent motion.

Results: Overall, as expected, children were more sensitive to coherent motion in the fast condition than the slow condition. Children with autism showed elevated motion coherence thresholds relative to typically developing children but only in the slow condition.

Conclusions: Rather than children with autism having pervasive difficulties in motion processing, these results suggest that they have a selective difficulty in extracting coherent motion information specifically at slow speeds. This pattern might be attributable to increased neural noise in children with autism due to undersampling of local motion signals, which may have a particularly pronounced effect on coherent motion processing in 'slow' motion channels. Understanding the effects of stimulus parameters

such as stimulus speed will be important for resolving discrepancies between previous studies that have found elevated motion coherence thresholds in autism and those that have not and also for refining theoretical models of altered perception in autism.

126.046 46 Evidence of Inaccurate and Inefficient Visual Speech Perception in Children with Autism Spectrum Disorders. T. Woynaroski*¹, R. A. Stevenson², J. K. Siemann¹, L. E. Dowell³, J. H. Foss-Feig⁴, M. Rivera¹ and M. T. Wallace¹, (1)Vanderbilt University, (2)Vanderbilt University Medical Center, (3)Oberlin College, (4)Yale University

Background: Speech perception is a complex multisensory process wherein visual information complements the acoustic stream to facilitate comprehension of linguistic meaning and communicative intent (Massaro, 1998). In typically developing (TD) individuals, visual cues speed the processing of speech information (van Wassenhove, Grant, & Poeppel, 2005) and improve the accuracy and efficiency of speech perception across listening conditions (Calvert, Brammer, & Iversen, 1998). Although prior work has noted differences in *detection*, *processing*, and *preference* of auditory speech stimuli in ASD (Bebko, Weiss, Demark, & Gomez, 2006; Gervais et al., 2004; Klin, 1991), mounting evidence suggests that children with ASD display impairments in *perception* of visual speech (Iarocci, Rombough, Yager, Weeks, & Chua, 2010; Smith & Bennetto, 2007; Williams, Whiten, & Singh, 2004; Woynaroski et al., in progress). Deficits in visual speech perception may contribute to the inefficient and inaccurate multisensory speech perception that has been observed in older children with ASD (Smith & Bennetto, 2007; Woynaroski, et al., in progress).

Objectives: This study examined speech perception in older children with ASD. Specific research questions included:

- a) Do children with ASD display deficits in identification of unisensory auditory or visual speech stimuli?
- b) Do children with ASD respond more slowly than TD peers to unisensory auditory or visual speech stimuli?

c) Do children with ASD display atypical audiovisual speech perception in comparison to TD peers?

Methods: Groups included 8 to 17 year-old children with ASD ($n=18$) and TD controls ($n=18$) matched for mean age, sex, and IQ. Participants viewed video recordings of a young woman speaking four CV syllables at a natural rate and volume with a neutral facial expression in unisensory visual, unisensory auditory, and audiovisual conditions. Instructions were unbiased (i.e., report what the speaker said), and the response mode was non-verbal (button-press). Stimulus presentation and recording of accuracy and reaction time data were managed by E-prime software.

Results: Children with ASD displayed impairments in their ability to identify visual speech stimuli when presented in a unisensory context. In contrast, no differences were found for identification of auditory speech stimuli. Additionally, the ASD group showed slower reaction times in response to unisensory visual stimuli, but not unisensory auditory stimuli, when compared with TD peers. Finally, the ASD group showed impairments in multisensory speech perception and atypical patterns of multisensory gain wherein they derived relatively greater benefit from auditory versus visual cues compared to TD controls.

Conclusions: Older children with ASD display inaccurate and inefficient perception of visual speech stimuli, but similar auditory speech perception skills, when compared with TD peers of similar age and cognitive ability. Inordinate deficits in the processing of visual speech perception may account, at least in part, for atypical patterns of multisensory speech perception in this population, and relate to broader symptoms of ASD. Findings are discussed in relation to previous work, prevalent theory, and future directions.

126.047 47 Hearing-in-Noise Perception in ASD. L. Bennetto^{*1}, P. D. Allen², J. DeSanctis¹, R. M. Nelson¹, A. Lord¹ and A. E. Luebke², (1)University of Rochester, (2)University of Rochester Medical Center

Background: The ability to filter relevant auditory information from background noise is critical for social communication, and impairment

of such filtering abilities is a commonly cited feature of autism spectrum disorder (ASD). Parents and teachers often report that children with ASD have difficulty attending to and understanding speech in noisy environments; these observations are supported by studies using standardized questionnaires of sensory functioning. While individuals with ASD have difficulties filtering speech in background noise, there may be variability in their abilities related to processing of the auditory target (e.g., speech vs. non-speech), the type of auditory background noise, and the ability of the auditory system to spatially separate the target from the background noise (spatial release from masking).

Objectives: We comprehensively characterized the nature of auditory filtering abilities in children with ASD compared to well matched controls, using both speech and musical tones as targets, speech-shaped noise and synthesized babble as maskers, and spatially matched or separated targets relative to background noise.

Methods: Children with ASD ($n=25$) and typically developing controls ($n=26$), ages 6 through 17, participated in this study. Groups were rigorously characterized via ADI-R and ADOS, and matched on age, gender, and verbal ability. Exclusion criteria included diagnoses of neurological or genetic disorders, and other conditions or illnesses that could affect hearing. Hearing was evaluated via audiometry; all subjects had thresholds <20 dB SPL for 500, 1000, 2000, and 4000 Hz, and <25 dB SPL for 8000 Hz.

Testing was conducted in a sound attenuated room, and included i) speech-in-noise intelligibility using the Hearing-in-Noise Test (HINT); and ii) forced-choice tonal perception-in-noise using the same protocol used for the HINT, but replacing speech with 3-4 tone differences. Control conditions included response to similar targets in quiet (which yielded no group differences).

Results: Children with ASD exhibited significantly impaired hearing-in-noise abilities compared to controls for speech targets ($p=.003$). This group difference persisted when the masking noise consisted of babble ($p=.01$). Importantly, children with ASD also demonstrated worse abilities relative to controls when targets were

musical tones ($p=.03$), suggesting that hearing in noise is not specific to language. Across all three conditions, the average signal-to-noise ratio for the autism group was roughly 2 dB higher than their matched peers. Children with ASD also showed no differences in spatial release from masking; both groups demonstrated the same pattern of better performance when the signal and noise were spatially separated.

Conclusions: These results confirmed significant impairment in hearing-in-noise across both speech and non-speech targets. Based on our findings, a newly developed forced-choice tone-in-noise test may be used to assess auditory filtering abilities in younger populations with ASD or those who have limited verbal abilities (who would therefore not be able to be tested using traditional speech-in-noise measures). This extension would then allow for further investigation of the specificity of auditory filtering impairment and its role in social-communicative functioning and language development across a broader age and ability span.

126.048 48 Increasing the Accuracy of Detection of Audio-Visual Integration Differences in Autism Spectrum Disorders. J. M. Bebko^{*1}, S. Oczak¹, L. N. Hancock¹, S. M. Brown¹ and J. J. A. Holden², (1)York University, (2)Queen's University

Background:

Individuals with autism often have difficulty integrating information across auditory and visual modalities (Bebko et al, 2006; Iarocci & McDonald, 2006). A commonly-used paradigm involves presenting 2 side-by-side visual displays, with an auditory track matched to only one display, while measuring the child's preferential looking toward the synchronized screen. Using this technique, Bebko et al. (2006) identified a deficit in the processing of speech specific audio-visual intermodal information in children with autism. In many previous studies, preferences are represented by only 60% looking rates, even though chance looking patterns are 50% with two screens. We introduced a modification using a 4-screen display and presented pilot data previously at IMFAR (Hancock et al., 2008). Better discriminability of looking patterns was found, since this methodology lowered chance looking probabilities to 25%, resulting in larger magnitudes of differences from chance. The present study further investigates precision of the

4-screen technique (with eye-tracking), using a larger ASD sample size and including a TD comparison group.

Objectives:

To assess the precision of the 4-screen versus 2-screen preferential looking paradigm (PLP). This is done in two stages. First, magnitude of effect (degree of difference from chance) on the 2- and 4-screen tasks for both ASD and TD groups is compared. Second, differences in looking patterns between ASD and TD groups are investigated using the 4-Screen PLP and eye-tracking data with linguistic and non-linguistic stimuli, and these results are compared with previous differences on 2-screen studies.

Methods:

23 children with ASD and 23 TD children between the ages of 3 and 12 years were tested. The 4-Screen PLP involved displaying four identical videos, offset in time, with an auditory track synchronous to only one of the videos. Videos contained either linguistic (L, person telling a story) or non-linguistic (NL, hand playing a piano) stimuli. Preferential looking is assessed from differences in total time looking at each screen.

Results:

Initial analyses indicate that the 4-screen variant produces more discriminable magnitudes of effect compared to chance: approximately 40% greater looking time at the preferred video over chance, vs. the 2-screen paradigm (approximately 10% greater than chance). Corrected for their relative chance levels (.25 vs .50), this is an *8-fold increase* in precision in the ability to detect preference, which represents a major advance in sensitivity for the paradigm. Two other results from previous two-screen studies were also preserved: First, for non-linguistic stimuli, both groups showed similar proportions of preferential looking to synchronous non-linguistic videos. In addition, we replicated the finding of an apparent speech-specific deficit in intermodal processing (IMP). Further analyses are ongoing.

Conclusions:

These findings demonstrate the strongly increased sensitivity of using a 4-screen over a 2-screen paradigm in detecting differences in preferential looking in ASD and TD children with audio-visual information. Often subtle differences occur, and the ability to detect them will enable a clearer understanding of variables contributing to the language difficulties in ASDs. The corroboration of our previous findings of an apparent speech-specific IMP difficulty in ASDs lends additional confidence to the paradigm.

126.049 49 Intact Auditory Processing but Impaired Speech Perception in Adolescents with Autism Spectrum Disorder and Early Language Delay. B. Boets*¹, J. Steyaert², J. S. Verhoeven¹, N. Rommel¹, I. Noens² and J. Wouters¹, (1)KU Leuven, (2)University of Leuven (KU Leuven)

Background: Language impairment and atypical sensory processing are often reported in autism spectrum disorders (ASD). In individuals with ASD, particularly in those with weak verbal abilities, an intriguing discrepancy has been observed between superior pitch processing and inferior auditory temporal and speech processing abilities. Studies in typically developing individuals (TD) have linked left hemispheric specialization for speech and language to an asymmetry in cortically auditory tuning: left auditory cortex is particularly sensitive to temporal aspects and faster modulations, whereas spectral aspects, like pitch, are preferentially processed in right auditory cortex. Against this background, it has been hypothesized that the pattern of superior pitch processing and impaired auditory temporal, speech and language processing in ASD may reflect superior right hemisphere versus inferior left hemisphere processing. Alternatively, it has been suggested that this pattern of assets and deficits could also be interpreted as evidence for the more domain-general Weak Central Coherence (WCC) or Enhanced Perceptual Functioning (EPF) theories of ASD.

Objectives: We assessed a broad range of low-level auditory and speech processing abilities, as well as general language skill, to investigate whether the observed pattern of assets and deficits favors the evidence for the Atypical Hemispheric Specialization hypothesis or rather for the WCC or EPF theories.

Methods: A series of psychophysical measures and language tasks were administered in 20 adolescents with ASD and early developmental language delay and 20 matched TD controls. Auditory measures were selected to preferentially target right auditory cortex (frequency discrimination, 4 Hz AM) and left auditory cortex processing (gap-in-noise detection, 20 Hz AM). Speech perception measures comprised the perception of words and sentences in various types of noise (i.e. stationary, fluctuating and babbling noise) to investigate the impact of increasing contextual information and spectrotemporal complexity of the background noise, respectively. Language measures comprised various phonological tasks and general expressive and receptive language tasks.

Results: Preliminary analyses confirmed that the ASD group shows severe and broad language impairments, as well as deficits in speech perception, in particular for sentence perception in spectrotemporally complex background noise. There were no group differences on any of the low-level auditory measures.

Conclusions: The pattern of superior spectral and inferior temporal auditory processing could not be replicated in this sample of adolescents with ASD and early language impairment. Given the similar performance in both groups, the obtained auditory profile could not be related to any advantageous or preferential hemispheric processing. Yet, the severe deficits in basic speech-in-noise perception are intriguing and point to an inability to efficiently integrate socially relevant auditory information.

126.050 50 Interpersonal Motor Interactions: Do Individuals with an Autism Spectrum Disorder Adjust?. C. M. Glazebrook*¹, D. A. Gonzalez² and J. L. Lyons³, (1)University of Manitoba, (2)University of Waterloo, (3)McMaster University

Background:

Interpersonal motor interactions (joint-action) occur on a daily basis. For example, when a friend passes you a cup of coffee, grasping the cup requires different preparation for each individual. In situations such as this, typically developing individuals plan their grip orientation to finish in a comfortable posture, even if it means adopting an uncomfortable posture earlier in the action sequence (i.e., end-state comfort; Rosenbaum,

1992). In joint-action situations typically developing individuals consider the end-goal of their partner and adjust their own movements to accommodate the other person (Gonzalez et al. 2011). The movement planning processes required for interpersonal motor interactions may be difficult for individuals with an Autism Spectrum Disorder (ASD) given the documented differences in performance on theory of mind and imitation tasks.

Objectives:

The goal of the present experiment was to determine if individuals with ASD exhibit end-state comfort behaviours similar to their typically developing peers in joint-action situations. Specifically, do individuals with ASD anticipate how another person will use an object and pass the object in a manner that facilitates the end-goal of the recipient?

Methods:

We replicated the tasks performed by Gonzalez et al. (2011) with a group of young adults with ASD (N=10; M=32.7 years). Participants were asked to either pass, place, or use three common tools: a wooden toy hammer, a stick, or a calculator. These tools were selected because the degree of affordance they offer (i.e., the physical characteristics they possess to prompt proper use) ranges from direct (hammer) to indirect (calculator). Participants were asked to pass the tool to a confederate who was either going to place the tool down, or use the tool for its intended task. Variables of interest included beginning and end-state grip orientations of both the participant and confederate (i.e., comfortable or uncomfortable) as a function of task goal, and the side to which the tool was placed or passed to (i.e., ipsilateral or contralateral).

Results:

Similar to Gonzalez et al. (2011), where typically developing young adults maximized their partner's end-state comfort by adopting personally uncomfortable passing postures, individuals with ASD also passed tools in a manner that facilitated comfortable end-use by the confederate. However, individuals with ASD

performed with greater variability compared to their typically developing peers. Individuals with ASD were most consistent using the stick or hammer, and most variable when using the calculator.

Conclusions:

The results of the present study provide evidence that the movement planning processes participants use to prepare to pass a tool are not stereotypical for individuals with ASD. We propose that performance on the interpersonal motor interactions reported here represent an important link between motor performance and more complex imitation or communication tasks.

126.051 51 Is Atypical Multisensory Integration in Autism Specific to Socially Contingent Information?. V. A. Bao*¹, L. Mottron², V. M. Doobay¹ and A. Bertone², (1)*Perceptual Neuroscience Laboratory for Autism and Development (PNLab)*, (2)*Centre d'excellence en Troubles envahissants du développement de l'Université de Montréal (CETEDUM)*

Background: The ability to use multisensory integration (MSI) (i.e., simultaneously integrate information from multiple sensory modalities) allows us to interact adaptively and efficiently with our surroundings by creating a unified and coherent internal representation of the external environment. Both empirical evidence and anecdotal accounts suggest that a decreased ability to integrate information from different senses may partially underlie sensory-related behaviors in autism (Iarocci & McDonald, 2006; Donohue et al 2012). The majority of the evidence supporting altered MSI in autism stems from studies using visual and auditory stimuli that are socio-communicative in nature, such as speech or human faces (Magnée et al 2008; Silverman et al 2010; Smith & Bennetto, 2007). It has been suggested that MSI deficits in autism may be limited to social stimuli, and that this effect may not generalize to low-level sensory information void of social or linguistic characteristics (Bebko et al 2006; Magnee et al 2008; Mongillo et al 2008).

Objectives: To assess MSI in autism using an auditory guided visual illusion task based on sensory information that is non-social in nature (i.e., beeps and flashes) in order to determine whether the purported MSI deficits in autism are generalizable to non-social stimuli.

Methods: Ten individuals diagnosed with ASD and ten individuals in a typically developing comparison group, matched for full-scale IQ, were asked to complete a computerized visual illusion task (Shams, Kamitani, & Shimojo, 2002) that assessed susceptibility to auditory-guided visual illusions. In this task, participants were required to determine whether they had perceived 1 or 2 flashes (F) while simultaneously hearing 0, 1, or 2 beeps (B). Participants were exposed to four non-illusion trials (i.e., 2F2B, 2F0B, 1F1B, 1F0B) and two illusion trials, whereby a discordant number of flashes and beeps were presented; (a) the fission illusion trial containing 1 flash and 2 beeps (1F2B), and (b) the fusion illusion trial containing 2 flashes and 1 beep (2F1B). Efficient MSI typically results in susceptibility to the illusion, with responses driven by number of beeps (B) presented (i.e., perceiving 2 flashes for the 1F2B fission trials). Susceptibility was measured for each group across illusion and non-illusion trials.

Results: A mixed-model ANOVA was conducted to determine if group-differences in illusion susceptibility (i.e., decreased accuracy for identifying number of flashes) existed across experimental conditions. Results indicated a significant decrease in accuracy for the illusory compared to the non-illusory conditions for both autism and control groups (i.e., the illusions are present). However, significant group differences were not found for any condition.

Conclusions: Comparable between-group performance on the auditory-guided visual illusion task used in the present study indicates that individuals with autism are able to efficiently integrate low-level, visual and auditory information that is void of social content (i.e., beeps & flashes). This result is consistent with the suggestion that atypical MSI in autism may be specific to situations that call for integrating socially laden information, such as faces and voices.

126.052 52 Motor Impairment in Autism Spectrum Disorders. J. Perrin*¹, C. Laranjeira², C. Buchert², M. Bouvard², T. Maffre¹, M. Huc-Chabrolle³, S. Roux⁴ and C. Le Menn Tripi⁵, (1)CHU de Toulouse, (2)CH Charles Perrens, (3)CRA Centre, CHRU de Tours, (4)UMR Inserm U930, (5)CHRU de Tours

Background: Although motor disturbances do not constitute a direct factor in an ASD diagnosis, they often impede the adaptation of persons with

ASD and play a part in their difficulties in achieving a satisfactory social integration. Efficiently dealing with such motor difficulties requires a better knowledge of the said disturbances.

Objectives: The aim of the present study is to get to know more precisely the frequency, intensity and characteristics of these motor disturbances throughout the whole spectrum, while also taking into account the diversity in intellectual level and symptom intensity. More largely, the point is to discuss the place of motor disturbances in ASD.

Methods: In order to answer these questions, a prospective multicentre study has been organized, involving several units for diagnostic and functional assessment attached to an Autism Resource Center (CRA Midi Pyrenees, CRA Centre, CRA Aquitaine). The ABC Movement (Henderson & Sugden, 1992) has been used to measure motor troubles both quantitatively (assessment of the level of motor impairment) and qualitatively (clinical characteristics having been listed thanks to the observation ABC-M checklist). We used ADOS, more particularly the Ghotam et al. algorithm (2007) to measure the intensity of autistic symptomatology. Lastly, cognitive level was assessed through several tools (Whesler scales (WPPSI, WISC), K-ABC, EDI-R).

Results: 70 children aged 4 to 12 were part of this study. The results show that, in accordance with our hypotheses, motor troubles in children with ASD are frequent and intense and affect the whole spectrum. Moreover, the level of motor impairment appears to be correlated with the cognitive level but seems independent from symptomatology intensity. Lastly, various motor profiles seem to have been distinguished.

Conclusions: Motor disorders appear to be a central feature in ASD. Taking into account this dimension in the evaluation and functional diagnostic appears fundamental to clarify the most effective therapeutic.

126.053 53 Multimodal Exploration in Children with Autism. A. Hellendoorn*¹, F. Altena¹, L. Wijnroks¹, P. Leseman¹ and E. Van Daalen², (1)Utrecht University, (2)University Medical Centre

Background: Skills develop in a multimodal context of people, objects and events that can be seen, heard and often felt (Smith and Gasser, 2005). Information emerging from multiple overlapping and time-locked sensory systems facilitates the detection of affordances in both the physical and social environment (Bahrick & Lickliter, 2000) and is therefore important for development.

Objectives: The purpose of this study was to examine multimodal exploration in young children with autism spectrum disorder (ASD) and to see whether children with ASD and children with other developmental delays/disorders (DD) without ASD differ in their multimodal exploration.

Methods: In this study 60 toddlers (30 with ASD) between the age of one and four years were included. Multimodal exploration was observed by applying a coding scheme to recordings of the ADOS using time sampling.

Results: The results show that the children with ASD display significantly less multimodal exploration (e.g. coordination feeling and looking at an object) compared to the children with DD. Moreover, the ASD group spends less time exploring the presented materials compared to the DD group. As hypothesized toddlers with ASD are less likely to explore multimodally and spend less time engaging with the presented materials.

Conclusions: Embodiment theory states that skills emerge in the interaction of the child with its environment and as a result of sensorimotor activity (Smith and Gasser, 2005). Children learn how to act upon their environment, the affordances of the environment, through exploration. Typically, this exploration is multimodal, information emerging from multiple sensory systems is overlapping and time-locked. Children with ASD may not only demonstrate less explorative behavior, their exploration seems to be more unimodal. This may affect the discovery of the affordances of the environment.

126.054 54 Multisensory Integration of Audiovisual Speech in Noise in Autism Spectrum Disorders. M. T. Wallace*¹, A. A. Shuster¹, J. K. Siemann¹, T. Woynaroski¹, S. E. Greenberg¹, S. M. Camarata² and R. A. Stevenson³, (1)Vanderbilt University, (2)Vanderbilt University Kennedy Center, (3)Vanderbilt University Medical Center

Background: Individuals with ASD exhibit atypical sensory processing spanning multiple sensory modalities (Iarocci 2006), including deficits in combining information across modalities (i.e., multisensory integration). Integrating sensory inputs into a single, unified percept is an important ethological process, leading to increases in perceptual accuracy, decreased response times, and increased rates of detection. These behavioral gains are particularly apparent when the signals are embedded in noise; the lower the signal-to-noise ratio (SNR), the greater the multisensory gain. Deficits in the realm of audiovisual speech integration have been shown in ASD (Bebko 2006, Kwakye 2011), which may be related to deficits in language and communication.

Objectives: The current experiment was designed to address the following questions:

- 1) Relative to matched controls, how well do individuals with ASD benefit in auditory comprehension from the addition of visual speech (i.e. being able to see the speakers mouth articulations)?
- 2) Is the impact of visual speech apparent at the level of whole words, or can benefits also be observed at the phonemic level.

Methods: Children with (N=12) and without ASD (N=12) were presented with single-word, tri-syllabic speech recordings in three sensory modalities: audio-only, visual-only, and audiovisual. All presentations were embedded in eight-speaker, multi-talker babble at an SNR of -6 dB SPL. Participants were given the option of identifying the word said either verbally or non-verbally (typed on a keyboard). Each response was scored on two measures:

- 1) Word recognition-Was the word correctly identified?
- 2) Phoneme recognition-What proportion of the three phonemes making up the words were accurately identified?

Finally, a McGurk paradigm was conducted, presenting unisensory and congruent audiovisual "ba" and "ga" utterances and a McGurk presentation of a visual "ga" paired with an auditory "ba." In the McGurk condition, the

percept of "da" or "tha" is frequently reported, indicating integration.

Results: Individuals with TD's recognition of audiovisual words in noise was significantly greater than their auditory-only scores (23% gain, $p < 0.001$). Individuals with ASD showed less benefit (11% gain, n.s.), with the addition of visual speech than did their TD counterparts ($p < 0.001$). On the phonemic level, this pattern persisted, with TD individuals showing 34% gain ($p < 0.001$) and ASD participants showing only a 1% difference (n.s.), and a significant difference between the two groups ($p < 0.001$). The McGurk effect also showed greater integration in the TD group than the ASD group (79% relative to 61%, $p < 0.05$).

Conclusions: Our everyday world is noisy, and an impaired ability to use multisensory cues to enhance the efficiency of linguistic and cognitive processing may have a significant impact on one's ability to interact with the world. Specifically, weaknesses in the ability of individuals with ASD to significantly bind auditory and visual speech signals may impact their language and communication abilities. Ongoing data collection with this study at other SNRs (-18 to 0 dB SPL) may provide further insights into possible differential impacts that noisy environments have on individuals with ASD

126.055 55 Strategies for Social and Nonsocial Visual Information Processing in Autistic Children and Adolescents. J. Guy*¹, C. Archambault¹, C. Habak², H. R. Wilson³, L. Mottron⁴ and A. Bertone⁴, (1)Perceptual Neuroscience Laboratory for Autism & Development (PNLab), (2)Centre de Recherche, Institut Universitaire de Gériatrie de Montréal, (3)Center for Vision Research, York University, (4)Centre d'excellence en Troubles envahissants du développement de l'Université de Montréal (CETEDUM)

Background: Individuals with Autism Spectrum Disorder (ASD) present both an atypical and distinctive visuo-perceptual profile (Mottron et al., 2006; Bertone et al., 2010). Despite marked social and behavioural impairments, individuals with ASD often excel at tasks requiring the local analysis of detailed information and preferentially attend to the constituent parts of a stimulus rather than its whole form. It remains unknown, however, whether a bias for such local analysis is at the origin of other aspects of the social cognitive phenotype in ASD, such as facial

information processing (Behrmann et al., 2006; Bertone et al., 2010, Weigelt 2012).

Objectives: To assess local and global visual processing strategies used during social (face identity discrimination task - Exp 1) and non-social (Navon task - Exp 2) visuo-perceptual tasks in the same group of autistic and non-autistic children and adolescents.

Methods: 30 autistic and 31 non-autistic children and adolescents (6-15 years) performed a face identity discrimination (Exp 1) and Navon task (Exp 2) under conditions favouring either a local or global analysis. In Exp 1, participants completed a socially-laden, facial identity discrimination task using synthetic, computer-generated face images (Wilson et al., 2002). These face images consisted of simplified (hair and skin texture removed), ecologically-validated stimuli, extracted from traditional face photographs in both frontal ("front") and 20° side ("side") viewpoints. Performance was measured using face identity discrimination thresholds for conditions where the target and choice faces were presented in the same view, biasing a local analysis (front-front or same-view condition), and in different views, biasing a global analysis (front-side or view-change condition) (Morin et al., 2012). Local and global visual processing for nonsocial information was assessed for the same participants in Exp 2 using the Navon task (Navon 1977): a local and global hierarchical, compound letter task. Participants completed a focused attention version of the task, where they responded to either local or global features of the stimuli in two separate conditions. Performance was measured in terms of accuracy and reaction time.

Results: Comparable between-group performances were found for the social, face identity discrimination task (Exp 1) in both local and global conditions. For the non-social, Navon task (Exp 2), the autism group performed significantly worse in the global condition, reflected by a higher error rate and slower average reaction time. When performance was assessed for the same participants across social and nonsocial tasks, decreased performance in the view-change condition of the face identity discrimination task was significantly correlated

with increased error rate in the global condition of the non-social, Navon task.

Conclusions: While the findings reveal a pattern of local precedence for non-social information processing only (Exp 2), correlations across social and nonsocial tasks suggest that autistics may use a similar strategy for the processing of both social and nonsocial information during childhood and adolescence. With ongoing data collection, we aim to further assess the role that development and/or experience may play in this relationship from the school-age years through to adulthood.

126.056 56 Tactile Reactivity in Children with and without Autism Spectrum Disorders. T. Tavassoli^{*1}, K. Bellesheim², M. Tommerdahl³, J. Holden³, D. Grodberg², A. Kolevzon², L. Bush⁴, S. Soffes² and J. D. Buxbaum², (1)Seaver Autism Center, Mount Sinai School of Medicine, (2)Mount Sinai School of Medicine, (3)University of North Carolina, (4)Seaver Autism Center

Background:

Anecdotal reports and questionnaire-based studies show that children with Autism Spectrum Disorders (ASD) experience sensory stimuli differently from typical developing children. The growing interest and role of sensory reactivity in ASD is reflected by the proposed changes to the DSM-V criteria, category B symptoms: "Hyper-or hypo-reactivity to sensory input or unusual interest in sensory aspects of environment". Tactile reactivity issues, such as being overwhelmed by touch, are commonly reported in ASD but have received far less attention than visual or auditory reactivity. Characterization of tactile reactivity with regards to behavior, perceptual thresholds, and associations to autistic traits is needed.

Objectives:

The current study aims to characterize tactile reactivity in children with and without ASD using parent reports, observations and psychophysical tests. Further we aim to investigate associations between tactile reactivity and autistic traits and empathy. Our objective is to compare n=20 children with ASD to n=20 typical developing children.

Methods:

So far participants have included 9 children with ASD and 4 typical developing children (6-12 years of age). Tactile reactivity was measured using a variety of tests. First, caregivers completed parent reports including the Sensory Profile. Second, observational measures, specifically the Sensory Processing Scales, were administered. Further, psychophysical tests varying in complexity were used; we measured simple and dynamic tactile thresholds, amplitude discrimination and temporal order judgments using a Cortical Metrics vibrotactile stimulator. Autistic traits were measured using the Autism Spectrum Quotient and empathy skills using the Child Empathy Quotient.

Results:

Preliminary results in the first 13 participants showed tactile reactivity differences in children with ASD compared to typical developing children ($p < .05$). Parents reported differences on tactile reactivity, and psychophysically measured thresholds differed between groups. In addition higher tactile reactivity (i.e. increased sensitivity to touch) was associated with higher autistic traits and less empathy.

Conclusions:

Children with ASD differ on various measures of tactile reactivity compared to typical developing children. Implications of a disparate tactile reactivity will be discussed as well as its associations to autistic traits and empathy. Tactile reactivity differences in children with ASD could be used to guide diagnosis and as a biomarker for treatment success.

126.057 57 The Influence of Distraction On Discrimination and Visuomotor Tracking in Sensory Deficient Processing & Autistic Children. J. A. Anguera^{*}, C. Rolle, S. Desai, A. Aitken, J. Gibbons, J. Harris, A. Gazzaley and E. Marco, University of California San Francisco

Background: Children with autism (ASD) and sensory processing disorders (SPD) are anecdotally reported to show difficulties with suppressing irrelevant sensory information. Recent work by our group and others suggests atypical cortical response to basic sensory information. Functional imaging work and structural connectivity assessment suggests

altered frontal-parietal connectivity in children with ASD and SPD. However the nature of the behavioral dysregulation is still not well understood, nor are there readily-available behavioral tools for use at home or at school that are inherently engaging while diagnostically valid. Furthermore, both the ASD and SPD clinical labels encompass a broad clinical phenotype with differences in distractibility and visuomotor control. Better understanding at an individual level will greatly facilitate treatment for all affected children.

Objectives:

This study seeks to investigate the ability to suppress visually distracting information in boys (8-11yo) with ASD, isolated SPD, and neurotypical controls. Furthermore, we looked to determine whether standard neuropsychology assessments, including those associated with visual attention, correlate with visuomotor tracking ability across diagnostic categories.

Methods:

All ASD participants (n=10) met lifetime ASD criteria based on ADI-R and ADOS evaluation. SPD participants (n=12) scored above the definite difference threshold for auditory and/or tactile behavior on the Sensory Profile but did not meet ADI-R/ADOS criteria for ASD. Controls (n=14) met neither ASD nor SPD criteria. We assessed cognitive and behavioral function using i) parent report measures of attention (child symptom inventory-CSI), ii) direct patient assessment with specific neuropsychology measures (motor speed, digit symbol & visual search), and iii) a custom perceptual discrimination video game (NeuroRacer) that requires visuomotor tracking under hierarchical distractibility demands.

Results: On the CSI, the control participants showed less behavioral inattention & hyperactivity than the other groups ($p < .05$). No group differences were observed on the motor speed task; however, the ASD and SPD cohorts demonstrated significantly slower speed of processing than the control cohort on the digit symbol task (each comparison: $p < .05$). On the visual search task, the ASD participants were less accurate than controls when finding target stimuli

amongst distractors ($p < .05$), with no differences between the SPD participants and either group ($p > .50$). While playing NeuroRacer during the visual distraction condition, we observed significant response time deficits to targets for the SPD group ($p < .005$) and similar trends in the ASD group ($p = .059$) versus the control cohort. Furthermore, we observed trends indicating impaired visuomotor tracking for both the ASD and SPD cohorts relative to controls ($p = .12$ and $p = .09$, respectively). When collapsing across groups, better visuomotor tracking during NeuroRacer correlated with visual search performance ($r = -.37$, $p < .05$).

Conclusions:

This study provides preliminary evidence that children with SPD and ASD are differentially impacted in the face of modality-congruent distraction for both visuomotor accuracy and reaction time. NeuroRacer visuomotor distractibility correlated with a standard neuropsychological measures of visual distraction, raising the possibility of using a 'fun', scientifically-inspired video game to characterize cognitive differences in children with neurodevelopmental challenges and potentially remediate these deficits with practice.

126.058 58 The Relationship Between Repetitive Behaviors and Sensory Behaviors in Children with Autism Spectrum Disorders. E. Drumm^{*1}, E. A. Kelley², L. O'Connell² and A. S. Li², (1)University of Toronto, (2)Queen's University

Background:

Repetitive behaviors are one of the three core symptoms of Autism Spectrum Disorder (ASD). Given the prevalence of repetitive behaviors, their diverse manifestations, and their potential to create profound functional impairment, the dearth of research on repetitive behaviors in ASD is surprising. Researchers tend to describe repetitive behaviors as maladaptive and occurring without reason (MacDonald et al., 2007; Matson & Dempsey, 2008). In contrast, many individuals with ASD describe repetitive behaviors as a way of coping with sensory processing (Yack, Sutton & Aquilla, 2003).

Sensory behaviors are well-associated clinical features of ASD. These behaviors are more

common in individuals with ASD than those with intellectual disability (Baranek et al., 2007; Rogers, Hepburn & Wehner, 2004). A recent study found that 88% of children with ASD have difficulties with sensory processing (Minshew & Hobson, 2008). Sensory behaviors may be related to patterns of repetitive behaviors in some individuals with ASD; however, empirical investigation into this relationship has been minimal. Separately, the presence of repetitive behaviors and the presence of sensory behaviors have been found to be inversely related to mental age in children with ASD (Baranek et al. 2007; Bishop, Richler, & Lord, 2006).

Objectives:

The current study was designed to extend the research on repetitive behaviors and sensory behaviors – particularly Boyd et al. (2009 & 2010), and Gabriels et al. (2008) – by quantitatively investigating their relationship while (a) employing a reliable measure of repetitive behaviors, the *Repetitive Behavior Scale-Revised (RBS-R)*, (b) employing a reliable measure of sensory behaviors, the *Sensory Profile*, (c) analyzing the subdomains of each measure, and (d) co-varying a consistent measure of cognitive ability.

Methods:

Data was collected from 35 children with ASD aged 3 to 11 years ($M = 6.4$ years, $SD = 2.2$ years; 29 males). Diagnostic status was confirmed by the *Autism Diagnostic Observation Schedule* – two children were excluded from analysis for not meeting the cut-off. Cognitive ability was measured using the *Differential Abilities Scales*. Our primary analysis examined correlations between repetitive behaviors, sensory behaviors, and autism severity as measured by the *RBS-R*, *Sensory Profile*, and *Social Communication Questionnaire*, respectively. Overlapping items between the three tests were removed.

Results:

A positive correlation was found between sensory behaviors and repetitive behaviors, $r(31) = .70$, $p < .001$, after partialling out mental age. No significant correlations were found between these

factors and autism severity. A correlation matrix was computed for the five *RBS-R* factors and six *Sensory Profile* processing domains. After correcting for multiple comparisons, this analysis revealed that reports of the factors *stereotyped behavior* and *ritualistic/sameness behavior* had the strongest correlations with sensory behaviors in this sample, over the factors *self-injurious behavior*, *compulsive behavior*, and *restricted interests*.

Conclusions:

This study found a significant relationship between parent-reports of sensory processing difficulties and repetitive behaviors in children with ASD, controlling for the effects of mental age: More frequent sensory behaviors related to more frequent and severe RBs. This study also suggests that *ritualistic/sameness behavior* and *stereotyped behavior* may have the strongest relationship with sensory behaviors.

126.059 59 Time Perception in the Autism Spectrum Disorders Across Sensory Modalities. A. Lambrechts*, S. B. Gaigg and K. Yarrow, *City University London*

Background: Autism Spectrum Disorder (ASD) is primarily defined by difficulties in social interaction and communication. The causes of these difficulties are likely to be multifaceted and recent research suggests that abnormal temporal processing might play a critical role (Allman, 2011). Studies of time perception suggest that individuals with ASD are as accurate but less precise than typically developing (TD) individuals (Falter et al., 2012; Allman et al., 2011; Martin et al., 2010) in discriminating or reproducing temporal durations in the sub-second to second range. Few studies, however, have examined multisensory time processing in ASD, which one would expect to be most relevant to the temporal dynamics of social interaction.

Objectives:

- Characterise time perception in ASD for durations relevant to social interaction

- Compare time perception in ASD in the visual, auditory and audiovisual modalities

Methods: We tested 24 ASD and 22 TD adults on a time comparison task involving auditory, visual and audiovisual stimuli. Participants were presented with pairs of stimuli (a standard and a probe), and asked to decide which lasted longer. The standard duration was either 800 or 1200ms, and the probes were either ± 5 , 10, 25 or 50% of the standard. Trials involving the 800ms and 1200ms standards were presented in pseudo-random order but trials were blocked by modality. In the visual modality the stimulus was a light grey square, in the auditory modality it was a 440Hz pure tone and in the audiovisual condition both stimuli were presented simultaneously.

Results: Half of the ASD individuals (N=12) performed very similar to the TD group, with participants overestimating probe durations in relation to the 800ms standard and underestimating them in relation to the 1200ms standard (as measured by shifts in the Point of Subjective Equality). In line with previous studies, the ASD group was less precise in their temporal judgements (as measured by the Weber Ratio, WR) and both groups demonstrated a lower WR in the visual as compared to the auditory and audiovisual modalities. However, the other half of ASD individuals (N=12) showed great difficulties with the task, particularly in the visual modality and for shorter durations. This latter group responded very quickly and follow-up measures are currently being collected to examine whether this might reflect heightened impulsivity and/or attenuated response inhibition. Importantly, across all ASD participants we observed a small but significant correlation between ADOS reciprocal-social-interaction scores and the extent to which individual data conformed to a discriminating as opposed to a chance performance profile.

Conclusions: Our findings suggest that time perception is partly preserved but less precise in ASD for durations that are critical for social interaction. The difficulties were most pronounced in the visual modality and for durations below 1 s and correlated moderately with ADOS reciprocal-social-interaction scores. Imprecise time perception may hinder the understanding of others' communicative behaviours and impact on speech-and-gesture coordination in ASD. Further studies are needed to understand what factors underlie the timing imprecision in ASD, and to

clarify the role of timing difficulties in social interaction and communication.

Genetic Factors in ASD Program

127 Genetic Factors in ASD

127.060 60 A Neurogenomics Approach to Study the Contribution of AUTS2 to Autism. L. M. Feldman^{*1}, G. Monderer-Rothkoff¹, E. Ben-David¹, E. Meshorer¹, M. Nissim-Rafinia¹, M. Groszer² and S. Shifman¹, (1)*The Hebrew University of Jerusalem*, (2)*Institut du Fer a Moulin*

Background: Autism susceptibility candidate 2 (AUTS2) was first identified as a possible risk gene for autism in a study of a monozygotic twin pair concordant for autism with a balanced translocation in the gene. Since then, translocations and copy number variations in AUTS2 have been identified in multiple individuals with autism and other neurodevelopmental phenotypes, including intellectual disability, seizures, short stature, cerebral atrophy and microcephaly. While it is one of the largest genes in the human genome, spanning over 1.2 Mb on chromosome 7q11.2, its function is yet unknown.

Objectives: The aim of this study was to uncover critical pathways involved in autism by investigating the molecular functions of AUTS2 and the effects of AUTS2 haploinsufficiency.

Methods: We studied the cellular localization and interactome of AUTS2, as well as the effects of perturbing the expression of this gene on global gene expression and neuronal differentiation. We performed a yeast two-hybrid assay and co-immunoprecipitation to identify proteins interacting with AUTS2. In vitro corticogenesis was used to study the effects of AUTS2 knockdown. We used expression microarrays to profile the transcriptome of knockdown cells during neuronal differentiation.

Results: We found that AUTS2 is a nuclear protein that is induced during the first stages of neuronal differentiation. Knockdown of AUTS2 during neuronal differentiation caused an increase in cell death and apoptosis. We also found that AUTS2 interacts with a polycomb group protein, explaining the changes in histone marks and the upregulation of polycomb target genes in heterozygous knockout cells. The regulatory network of AUTS2 was enriched for common variants that increase the risk of autism.

Conclusions: Our results suggest that AUTS2 is involved in transcriptional control during neuronal differentiation as a part of a polycomb complex. Knockdown of AUTS2 increase cell death during neuronal differentiation and could explain the microcephaly and cerebral atrophy phenotypes observed in individuals with mutations in AUTS2. The findings also suggest that AUTS2 regulates other genes that may function as risk genes for autism. As such, AUTS2 can provide a valuable entry-point to the understanding of neural pathways relevant to autism and other neurodevelopmental disorders.

127.061 61 Analysis of Cognitive Performance, Social Functioning, and Body Mass Index As Quantitative Rather Than Dichotomous Traits in Individuals with Deletion 16p11.2. A. Moreno De Luca*¹, P. T. Orr¹, S. M. Myers¹, T. D. Challman¹, D. W. Evans², R. P. Goin-Kochel³, E. Hanson⁴, R. Bernier⁵, L. Green-Snyder⁶, J. E. Spiro⁷, W. Chung⁸, J. N. Constantino⁹ and D. H. Ledbetter¹, (1)*Bucknell University*, (2)*Geisinger Health System*, (3)*Baylor College of Medicine*, (4)*Children's Hospital Boston*, (5)*University of Washington*, (6)*Boston Children's Hospital*, (7)*Simons Foundation*, (8)*Columbia University Medical Center*, (9)*Washington University School of Medicine*

Background: The recurrent deletion 16p11.2 is the second most common pathogenic copy number variant identified among individuals with neurodevelopmental disorders. It was initially identified in subjects with autism and/or intellectual disability (ID) and subsequently associated with macrocephaly, obesity, seizures, speech and motor delays, congenital anomalies, and paroxysmal kinesigenic dyskinesia. Deletion carriers show substantial clinical heterogeneity, including apparently normal individuals, an observation often interpreted as evidence of incomplete penetrance.

Objectives: To evaluate in a quantitative manner the impact of deletion 16p11.2 on autism features, social functioning, cognitive abilities, and body mass index.

Methods: We studied 30 individuals with *de novo* del 16p11.2 from the Simons Variation in Individuals Project and their non-carrier parents (n=58) and siblings (n=19). We examined parent reports from the Social Responsiveness Scale (SRS), a quantitative scale that evaluates social awareness, reciprocal social communication, social information processing, and social anxiety,

resulting in a T-score ranging from 30 (highly sociable) to 90 (severe social impairment) with a mean of 50 and a standard deviation (SD) of 10. SRS scores are highly heritable, commonly unrelated to intelligence quotient (IQ), and continuously distributed in the general population. We also evaluated full-scale IQ (FSIQ), a quantitative measure with a mean of 100 and a SD of 15, and body mass index (BMI), a proxy for human body fat based on an individual's weight and height.

Results: Within this group, 32% of probands met full criteria for autism spectrum disorders using categorical diagnostic tools (ADI-R and ADOS). For the SRS, the mean T-score for probands was 71.9 compared to 46.8 in parents, and 44.7 in siblings. Moreover, scores in probands correlate with paternal scores (Spearman: $\rho(20) = .56, p = 0.1$). Therefore, this quantitative trait revealed a 2.2 SD shift of mean SRS scores of probands relative to unaffected intrafamilial controls ($p=4.44 \times 10^{-16}$). These results are very similar to those obtained using FSIQ to assess cognitive functioning in this subset of cases: 16.6% met a categorical diagnostic criteria for ID (FSIQ ≤ 70); however, if viewed as a quantitative trait, FSIQ was 1.8 SD lower in probands compared to their parents ($p=6.66 \times 10^{-16}$) with a significant correlation between proband and maternal scores (Spearman: $\rho(29) = .43, p = .01$). Finally, proband BMI z-scores were found to be 0.74 SD higher than parental scores and positively correlated with paternal BMI (Spearman: $\rho(24) = .55, p = .005$).

Conclusions: By using continuous, quantitative traits such as FSIQ, SRS, and BMI scores to compare probands with their unaffected, non-carrier relatives, rather than using categorical variables such as DSM diagnoses or qualitative, dichotomous traits (i.e., normal vs. abnormal), we showed that parent-reported social behavior, cognitive function, and BMI are significantly impacted in a deleterious fashion among children with deletion 16p11.2 when compared to non-carrier relatives. These data may be more consistent with phenotypic heterogeneity related to genetic/family background rather than evidence of incomplete penetrance.

127.062 62 Cell Type Enrichment Analysis to Identify Cellular Targets for Autism Spectrum Disorder. X. Xu¹, A. Nehorai²

and J. Dougherty*¹, (1)Washington University, (2)Washington University

Background: The brain is the most complex organ of the entire body containing hundreds of distinct cell types, each with unique morphologies, projections, functional roles, and gene expression profiles. Yet, there are clear examples of neurological disruptions caused by deficiencies in just one cell type or circuit. However, the cellular disruptions that lead to the behavioral abnormalities in autism are not clear. If there were a method to identify the cell types that serve as the intermediaries between a set of genetic lesions and a particular behavioral disruption, then one could identify cellular targets for treatment. Importantly, there is a remarkable diversity of gene expression across the nervous system. We hypothesize that across a large number of candidate disease genes implicated in a disorder, we may be able to identify the vulnerable cell type(s) by a relative overabundance in their expression of candidate disease genes.

Objectives: To leverage human genetic and cell type specific gene expression information to identify cells and circuits that are likely to be disrupted in autism spectrum disorders.

Methods: High-throughput methods have identified dozens of candidate genes that may contribute to disorders, utilizing common variant genome-wide association studies, rare variant analyses (such as exome sequencing and copy number variation), and postmortem gene expression analysis of patient brains. In previous work, we generated dozens of 'bacTRAP' transgenic mouse lines specifically with the goal of systematically examining the gene expression profiles in targeted cell types. Here, we combine these two sources of information and test an approach for allowing the selective expression of genes to guide us towards the neurobiology of disorder. We test two statistical methods, a non-parametric approach and permutation based approach, for identifying cell types by the intersection of gene expression with disease gene information. As a likely positive control for the method, we include retinal cell type gene expression and candidate gene lists derived from dominant and recessive forms of human retinopathies. As a negative control, we include candidate gene lists for genes that influence

height, which should be unrelated to cell specific gene expression in the brain.

Results: Our approach successfully identifies a robust enrichment of Rod and Cone expressed genes in human retinopathy disease genes, and no enrichment in any cell types for genes related to height. Analysis of patient post-mortem gene expression data and candidate gene lists from human genetic studies both indicate a common feature of autism may be the disruption of cortical interneurons. Some modestly significant signal was also seen in corticothalamic and striatal cell types after multiple testing correction. There was no enrichment signal for other autism candidate regions or cells, for example, in any cell type of the cerebellum.

Conclusions: We have developed a novel approach to identify potential cellular mechanisms mediating psychiatric disorder, and identified candidate cell types that may mediate features of autism spectrum disorders. We hope that our identification of candidate cell types from the genetic information may suggest new targets for treatments.

127.063 63 Combined Analysis of Exome Sequencing Points Toward a Major Role for Transcription Regulation During Brain Development in Autism. E. Ben-David* and S. Shifman, *The Hebrew University of Jerusalem*

Background: Four recent studies of the coding regions of the human genome (the 'exome'), suggest that new (de novo) mutations in hundreds of genes may contribute to the risk of autism spectrum disorder (ASD). While the experimental strategy in the different efforts is almost identical, the four studies were published independently, and no integrative analysis has yet been reported. Notably, limited conclusions regarding the specific systems of genes disrupted by de novo mutations can be drawn based on each study alone. This stems from the relatively small fraction of mutations identified in each study in which there is a clear functional phenotype at the protein level.

Objectives: We performed an integrative meta-analysis of the four studies, to uncover systems of genes affected by de-novo exonic mutations in ASD.

Methods: We first focused on genes containing nonsense, frameshift, or splice site de-novo mutations. To characterize the genes, we analyzed the enrichment of cellular processes and gene ontology (GO) using the Database for Annotation, Visualization and Integrated Discovery (DAVID). We then used a published dataset of brain gene expression throughout different life stages, to cluster the genes based on their expression during the developmental stages of the human brain. To cluster the genes we performed a Weighted Gene Co-Expression Analysis (WGCNA). We then broadened our scope by including non-synonymous substitutions, and performed a protein-protein interaction analysis using the Disease Association Protein-Protein Link Evaluator (DAPPLE).

Results: Among the genes with disruptive mutations, we found a significant enrichment for "chromatin regulator". This enrichment was significant compared to a large control exome sequencing cohort, as well as compared with the silent mutations in the same individuals, strongly supporting its specificity to ASD. When clustering the genes based on their expression during brain development, the chromatin regulator genes were mostly clustered in a large module of genes which is strongly expressed prenatally, with a sharp decrease in expression after birth. In contrast, silent mutations were significantly less likely to be in genes highly expressed prenatally. Finally, to test the interactions at the protein level, we included the non-synonymous mutations, and performed a protein-protein link analysis using DAPPLE. This analysis found a significant connectivity between the genes, and identified a list of strongly interacting genes, which was also highly enriched for genes involved in chromatin regulation.

Conclusions: While it has been proposed that the origins of ASD are at the synapse, our meta-analysis of de novo mutations shows that the many of the recently identified mutations are in genes that are involved in transcriptional regulation, specifically chromatin related proteins, which are active during brain development. These findings, together with the association of other genes in this category with autism and intellectual disability, highlight the need to further study this type of genes as risk factors for ASD.

127.064 64 De Novo Mutation of the Dopamine Transporter (DAT) Gene in Autism Reveals a Novel Component of ASD Pathogenesis. N. G. Campbell*, P. J. Hamilton, K. B. Erreger, A. N. Belovich, H. Matthies, A. Galli and J. S. Sutcliffe, *Vanderbilt University*

Background: Risk for ASD is largely genetically determined, however, ASD genetic architecture is highly complex. Studies focusing on rare DNA copy number variation (CNV) point to *de novo* mutation as one important class of genetic liability. Recently, whole exome sequencing (WES) has become a focus of genetic studies in ASD, has implicated numerous genes and strongly underscored the extreme heterogeneity of ASD risk. Several groups have conducted WES on large case-control samples and families. Among the first *de novo* coding mutations (DNMs) identified by the NIH ARRA Autism Sequencing Consortium was a missense substitution (T356M) in the *SLC6A3* gene encoding the dopamine (DA) transporter (DAT). DAT functions presynaptically to uptake DA released into the synapse, thus regulating synaptic [DA] and signaling to postsynaptic receptors. Previous studies have documented association of a rare, functional DAT variant with ADHD, which co-occurs in ~40% of people with ASD.

Objectives: To characterize functional impact caused by T356M, we sought to use both *in vitro* and *in vivo* systems to evaluate its effect on DAT function and regulation.

Methods: Wildtype and T356M mutant DAT expression constructs were transfected into heterologous Chinese hamster ovary (CHO) cells to measure DA uptake and, using the electrophysiological technique amperometry with patch-clamped cells, the ability of DAT to efflux DA into the extracellular space when treated with amphetamine (AMPH); DA efflux is a property of the wildtype transporter. *In vivo* analysis of wildtype and T356M DAT employed a "humanized" *Drosophila* harboring the WT (or knock-in mutant) human gene replacing the endogenous gene. Initial studies focused on locomotion in these models.

Results: Significant cross-species conservation of the T356 residue and use of prediction algorithms suggested that this missense variant would have a damaging effect on the protein. Expression

of T356M DAT in CHO cells revealed a substantial reduction, near absence, of DAT-dependent DA uptake relative to wildtype ($p < 0.001$). Remarkably, application of $10 \mu\text{M Zn}^{2+}$ partially restored reuptake activity of T356M DAT compared with mutant DAT expressing cells without Zn^{2+} supplementation. Patch-clamp experiments pre-loading cells with DA revealed significantly diminished AMPH-induced DA efflux by T356M DAT relative to wildtype ($p < 0.01$). Most notably, amperometry experiments revealed that mutant DAT *constitutively* leaks DA from the cell under basal conditions, contrary to wildtype transporter. Lastly, *Drosophila* containing the T356M knock-in mutation, compared with those containing wildtype DAT, show significantly increased basal locomotion across the 12-hour light cycle ($p < 0.05$). This behavior is similar to the hyperactivity observed in DAT null *Drosophila*.

Conclusions: We have characterized a novel DNM affecting DAT that demonstrates profound functional abnormalities. Given the powerful constitutive efflux of DA and virtual absence of DA uptake activity caused by the mutation, we consider it likely that this DNM is a significant ASD risk factor. Taken together with prior association between abnormal DAT function and ADHD, these observations may provide a link between ASD risk and pathophysiology and ADHD. These studies also more broadly implicate altered regulation of DA homeostasis as a potential mechanism underlying part of the overall liability to ASD.

127.065 65 Disentangling the Heterogeneity of Autism Spectrum Disorders: The Identification of 'Signature' Behavioural Phenotypes Derived From Specific Genetic Syndromes. H. Bruining^{*1}, R. J. Eijkemans¹, M. J. Kas¹, S. R. Curran², J. A. Vorstman¹ and P. F. Bolton³, (1)Brain Centre Rudolf Magnus, (2)Kings College London, (3)Institute of Psychiatry, King's College London

Background: Aetiological and phenotypic heterogeneity in autism spectrum disorder poses major challenges to mapping causal pathophysiological pathways.

Objectives: In order to disentangle this heterogeneity, we conducted a 'proof of principle' study to test the hypothesis that there exist 'signature' autism behavioural phenotypes that index underlying genetic risk and that these behavioural profiles can be used to help disentangle heterogeneity.

Methods: We tested the specificity autism behavioural phenotypes using Support Vector Learning Machine Analysis (SVM) on samples comprising six different genetic syndromes that carry an increased risk for autism spectrum disorder: 22q11.2 deletion syndrome, Down's syndrome, Prader Willi syndrome, Supernumerary Marker chromosome 15, Tuberous sclerosis complex and Klinefelter syndrome ($n = 322$, groups ranging 21-90).

Results: The SVM analysis of items from the autism diagnostic interview identified syndrome specific behavioural phenotypes with 63 % accuracy (compared to random accuracy of 23%). We next tested whether these 'signature' behavioural phenotypes could be identified in idiopathic cases of autism spectrum disorder and whether they exhibited a liability to familiarity, by analyzing autism diagnostic interview items from families collected as part of the Autism Genetics Resource Exchange (AGRE). These analyses indicated that the signatures behavioural profiles occurred significantly more often than random expectation, with 63% of probands exhibiting the signature behavioural profile associated with Tuberous Sclerosis Complex. Furthermore, examination of the profiles in the probands siblings indicated that the 'signature' behavioural phenotypes exhibited significant familiarity.

Conclusions: These results indicate that genetic disorders associated with autism spectrum disorders exhibit distinctive behavioural phenotypes and that similar 'signature' phenotypes exist in cases with idiopathic autism spectrum disorder and that these 'breed true' within families. Together the findings indicate that heterogeneity in the behavioural manifestations of autism spectrum disorder index the nature of the underlying genetic risk in pathophysiology. These approaches provide a conceptual approach to disentangling heterogeneity and subtyping cases for more personalized treatments.

127.066 66 From Autism to Schizophrenia: Study of the Genetic Mechanisms Underlying Brain Dysfunction and Structural Phenotypes in Schizophrenia and Autistic Spectrum Disorders. the Ausz_[Eucan] Project. ERA-NET Neuron. M. Fatjo-Vilas^{*1}, L. Pina-Camacho², M. Parellada², L. Boada², C. Prats¹, G. A. Rouleau³, K. Nave⁴, M. O. Krebs⁵ and L. Fañanas¹, (1)Universitat de Barcelona. Unitat

d'Antropologia, Facultat de Biologia, (2)Child and Adolescent Psychiatry Department, CIBERSAM, Instituto de Investigación Sanitaria Gregorio Marañón, IiSGM, Hospital General Universitario Gregorio Marañón, (3)Université de Montréal. CHUM Research Centre, (4)Max-Planck-Society ; Max-Planck-Institute for Experimental Medicine; Dpt. Neurogenetics, (5)INSERM Université Paris Descartes, Hôpital Sainte-Anne Laboratoire de Physiopathologie de Maladies Psychiatriques, LPMP

Background:

There is a great deal of recent direct and indirect genetic data showing clinical and biological links between schizophrenia (SCZ) and autism spectrum disorders (ASD). Specifically, various candidate gene and linkage analyses as well as studies of copy number variants (CNVs) have yielded a handful of genes that seem to be involved in both diagnoses. Many of the proteins related to these psychosis candidate genes contribute, in a convergent and complementary manner, to the plasticity of synapses. Such convergence suggests that the main neurochemical deregulations in SCZ and/or ASD may lead to or be associated with inefficient control of cortical input onto subcortical striatal dopamine, as well as inefficient cortico-cortical connectivity and function. Despite their high potential interest, the contribution of white matter (WM) proteins (and their genes) in these causative pathways have been less extensively studied than grey matter (GM) related genes. We hypothesize that: i) genetic variability of WM related genes will be associated with ASD and SCZ, and ii) some genetic variants will be specifically associated with ASD and early-onset SCZ (E-SCZ) but not with adult-onset forms of psychosis.

Objectives:

The specific aims are: i) to analyze single nucleotide polymorphisms (SNPs) in WM related genes in samples of ASD and SCZ patients, their relatives, and healthy subjects, ii) to explore the relationship of these genetic variants (SNPs or haplotypes) to particular WM phenotypes obtained by MRI studies, and iii) to identify genotypic-phenotypic relationships underlying the similarities and dissimilarities among these disorders, placed along the impaired neurodevelopment continuum.

Methods:

The AUSZ_[EUCan] project is a collaborative European project, funded by the Network of European Funding for Neuroscience Research – ERA-NET NEURON, that proposes an integrative approach to SCZ and ASD, with a special focus on WM abnormalities. Candidate gene-wide genotyping will be performed on the already available ERA-NET blood samples (from patients with early- and adult-onset SCZ or ASD, their relatives, and healthy subjects). This approach will be taken in three independent Caucasian population-based samples from France and Spain (n=2000).

The selected candidate genes include those involved in myelin structure, oligodendrocyte development, synaptic plasticity and axonal regeneration, transcription and signalling factors and cell adhesion molecules and receptors (e.g. MAG, CNP, MBP, QKI, NOGO, OLIG2, NRXN1), all putatively involved in the etiology of SCZ and ASD. The selection of tagSNPs was based on the HapMap CEU population to cover the genetic variability of these genes. In addition, the known and predicted interactions of the proteins encoded by the selected genes have been taken into account in order to construct a candidate gene network and perform interaction analyses among them.

Results:

The genotyping will be conducted in two phases: the first in late 2012 and the second in 2013. The first phase will allow the genotyping of 128 SNPs in 15 genes in 2000 subjects using the TaqMan OpenArray® Real Time PCR System. Here we will present the preliminary results of the first genotyping phase.

Conclusions:

Candidate gene analyses may help to identify WM related genes associated with ASD and SCZ.

127.067 67 Looking to the Left or Looking to the Right? Revisiting Visual Scanning of Faces in Young Children with ASD. Q. Guillon^{*1}, S. Baduel¹, N. Hadjikhani² and B. Roge¹,
(1)University of Toulouse, (2)EPFL

Background: Behavioral and neuroimaging studies have demonstrated a right hemisphere advantage in face processing, manifested by a left gaze bias (LGB) when participants look at faces (i.e. visual input come from left visual field). This tendency to look first and for longer periods at the left hemiface (from the viewer's perspective) appears to develop between 6 and 12 months of age. The LGB has been observed not only for human faces, but also for dog faces in a group of 4-year-old typically developing children. To date, much of the studies investigating visual scanning of faces in ASD have focused on looking-time towards the mouth and eyes regions. However, two studies have recently found that adults with ASD as well as children at risk for ASD spend less time looking at the left side of a face than control participants. Whether this lack of LGB is also present for the direction of the first fixation, a measure reflecting the right hemisphere bias, and overall, whether a lack of LGB is specific to human faces in young children with ASD remains unknown.

Objectives: To determine if young children with ASD demonstrate the typical LGB for the first fixation while looking at human faces and to determine the specificity of a lack of LGB.

Methods: Eye-tracking data were collected while young children with ASD (24- to 60-months old) and typically developing children (24- to 60-months old) viewed picture of human faces and of dog faces. For each participant and each picture category presented, the direction of the first fixation and the total fixation time on each side of the face were analyzed, and Laterality Index (LI) was computed. LI (first look) and LI (total fixation time) were compared between diagnostic groups for each picture category separately.

Results: Preliminary results suggest that the ASD group differ significantly from the TD group. As expected, typically developing children demonstrate the typical LGB for both human and dog faces. To the contrary, ASD children do not show such an effect for any of the face category presented. At an individual level, some of the young children with ASD even present an opposite bias, and notably exhibit a higher probability of first gaze towards the right side of the face.

Conclusions: These results suggest that a lack of LGB for the direction of the first fixation may be considered as an eye-tracking marker for ASD. Overall, these results are discussed in terms of their potential use in a screening program for ASD in a general population setting.

127.068 68 Evidence Uptake in Early Identification of Autism in Community-Based Settings. K. Shikako-Thomas^{*1}, A. Yussuf¹, D. Maynard², R. Birnbaum³ and M. Elsabbagh¹, (1)McGill University, (2)Canadian Association of Pediatric Health Centers, (3)Montreal Children's Hospital

Background:

Several early identification tools and guidelines for screening have been developed in the recent years for autism. Nevertheless, there is a wide gap in uptake and implementation of such information by frontline clinicians, which often causes delays in diagnosis and referral for early intervention.

Objectives:

The goal of the current study was to understand barriers to uptake of evidence among front-line practitioners and to identify evidence-based strategies that could support informed decision-making among service providers in addressing the needs of families affected by autism.

Methods:

A scoping review was performed to comprehensively identify guidelines and studies addressing early screening and identification of autism and other neurodevelopmental disabilities in children ages 0 to 5 years old. Databases reviewed included CINAHL, Medline, Embase, PubMed, PsycInfo and open access archives such as Google Scholar and Government sources (e.g. Canada Health). Search terms exploded on keywords and Mesh terms related to knowledge translation and exchange, evidence-based practice, early identification and developmental disabilities. Barriers to use and adherence of existing guidelines by frontline clinicians (i.e. paediatricians, general practitioners and family physicians) were identified. Strategies that were demonstrated to be successful in optimizing use of evidence were extracted.

Results:

In the scoping review, we identified lack of time or skills among front-line practitioners to appraise literature and understand research evidence as the main barrier to evidence uptake.

Disseminating knowledge of guidelines through activities to inform clinicians of current evidence (e.g. resource guides), developing other easy-to-access materials (e.g. checklists, screening tools), and improving communication between physicians and families may be fundamental to facilitate the early identification of autism. A follow-up national Canadian survey is currently underway to clarify the gaps in the use of evidence. This survey will generate a list of effective strategies to promote evidence-based early identification of neurodevelopmental disabilities that researchers and service providers can use to facilitate communication between research-based evidence and frontline practice.

Conclusions:

The early identification of autism can be facilitated and promoted by front-line clinicians in community settings. However, these professionals often face several barriers to the uptake of research-based evidence that could support the early identification process and promote early interventions that would ultimately result in better outcomes for this population. Knowledge of barriers and facilitators to the use of evidence may facilitate the knowledge translation process from researchers to front-line clinicians in order to communicate the latest research findings and promote best practices.

127.069 69 Identification of Rare Recurrent Genetic Variants in High-Risk ASD Families and Their Role in a Large ASD Case/Control Population. C. Hensel^{*1}, N. Matsunami², D. D. Hadley³, B. Christensen⁴, C. Kim³, K. Thomas³, R. Pellegrino³, J. Stevens², L. Baird², B. Otterud², K. S. Ho¹, T. S. Varvil², T. Leppert², C. G. Lambert⁴, M. Leppert² and H. Hakonarson³, (1)*Lineagen, Inc.*, (2)*University of Utah*, (3)*Children's Hospital of Philadelphia*, (4)*Golden Helix, Inc.*

Background: Genetic variation plays a significant etiological role in autism spectrum disorders (ASDs), and numerous studies documenting the relevance of copy number variants (CNVs) and single nucleotide variants (SNVs) in ASD have been published.

Objectives: This study was designed with three goals in mind. The first goal was to identify CNVs present in high-risk ASD families and to determine which of those CNVs contribute etiologically to ASD in the general population. The second goal was to confirm the findings of several published ASD CNV studies using a larger case/control population, to determine the potential clinical utility of those CNVs in the genetic analysis of children with ASD. The third goal was to determine if any SNVs identified as potential risk variants in high-risk ASD families supported their potential role as risk alleles in same case/control population.

Methods: CNVs in high-risk ASD families were identified using the Affymetrix Genome-Wide Human SNP array 6.0. SNVs were identified by sequence capture in regions of genetic linkage and in published ASD candidate genes. CNVs and SNVs subsequently were evaluated in a set of 3000 ASD cases and 6000 controls using a custom Illumina iSelect array followed by molecular confirmation of significant variants.

Results: We identified 153 putative ASD-specific CNVs in 55 affected individuals from 9 multiplex ASD families. These CNVs were not observed in control samples from three generation Utah CEPH families. Our case/control analysis revealed that 14 CNVs from high-risk ASD families were observed in unrelated ASD cases and had at least suggestive evidence for a role in ASD etiology. We also identified CNVs not detected in our high-risk families using SNVs probes that we placed on the array, suggesting that some genetic regions can be impacted at both the structural and sequence levels. Findings for published CNVs indicated that many appeared to increase the ASD risk only slightly, since these CNVs also were found in many control DNA samples. One rare SNV was observed in two unrelated ASD cases and in none of the 6000 controls, suggesting that variants in this gene may be risk factors for ASD.

Conclusions: Genetic variants identified in high-risk ASD families also appear to play a role in ASD etiology in unrelated ASD cases. The absence of 10 of these variants from public ASD databases suggests that they represent previously unidentified risk variants. These variants lay the groundwork for the development of a more

sensitive test to use in the genetic evaluation of children with ASD.

127.070 70 Insights Into the Role of Contactin 4, -5 and -6 in Autism Spectrum Disorders. I. Cloez-Tayarani*¹, O. Mercati¹, A. Danckaert², G. André-Leroux³, M. Bellinzoni³, L. Gouder¹, K. Watanabe⁴, Y. Shimoda⁵, R. Delorme⁶, M. Leboyer⁷ and T. Bourgeron⁸, (1)*Institut Pasteur CNRS URA 2182*, (2)*Institut Pasteur*, (3)*Institut Pasteur CNRS URA UMR3528*, (4)*Nagaoka National College of Technology*, (5)*Nagaoka University of Technology*, (6)*Hôpital Robert Debré*, (7)*INSERM U 955, Hôpital Chenevier-Mondor*, (8)*Paris Diderot University*

Background: Autism spectrum disorders (ASD) are a heterogeneous group of severe developmental disorders. A strong genetic component contributes to the aetiologies of ASD, which may vary from monogenic forms of ASD with the presence of *de novo* mutations to oligo – and polygenic forms with the interaction of multiple hits within the genome. We have previously shown the involvement of genes encoding proteins involved in the formation and maintenance of synapses such as the Neuroligin-Shank-Neurexin pathway, with rare variants having a strong effect found in a relatively limited number of families.

Objectives: We focused our study on contactins (CNTNs), a family of six cell adhesion proteins of the immunoglobulin superfamily which are involved in brain development, neuronal wiring, and promote neurite outgrowth *in vitro*. Our genetic studies have led to the identification of copy number variations as well as non-synonymous rare variations in *CNTN4*, *CNTN5* and *CNTN6* genes in patients with ASD, and also in control individuals. Most of these variants were inherited from healthy parents. For *CNTN5* and *CNTN6*, the identified mutations are distributed among the immunoglobulin and fibronectin domains of CNTN molecules. For *CNTN4*, we observed a single stop mutation located in the first fibronectin-like domain, leading to a truncated protein. We investigated the effects of wild-type and mutated rat Cntn4, Cntn5 and Cntn6 on different aspects of neurite outgrowth. In a second set of experiments, we analyzed the molecular interactions of human PTPRG and human *CNTN4*, -5, and -6 by generating the respective 3D structures of each complex, respectively. We then tested the effects of mutations located in the first four Ig-domains of

CNTN5 and *CNTN6* on the 3D structures of these proteins.

Methods: We set up a co-culture system using rat cortical neurons and HEK293 cells over-expressing and delivering the secreted forms of wild-type and mutated rat contactin4, -5 and -6 in the vicinity of neurons. The molecular interaction of CNTN with PTPRG was studied using homology modeling and protein docking calculations.

Results: Our results show different promoting effects of wild-type rat Cntn4, Cntn5 and Cntn6 on neurite outgrowth and branching. We also observed significant differences, at the crucial Ig2-Ig3 domains, in the structure of human *CNTN5* and *CNTN6* as compared to *CNTN4*, with no direct consequence on PTPRG binding. The functional screening of contactin mutations identified in patients with ASD revealed significant alterations in the neurite outgrowth properties as compared to wild-type contactin proteins.

Conclusions: Our data suggest that the differential contactin effects on neurite outgrowth do not result from distinct interactions with PTPRG. Results from our mutational screening indicate that rare variations of the contactins might represent inherited risk factors for ASD.

127.071 71 Simons VIP: Expanding the Characterization of 16p11.2 Deletion Syndrome. E. Hanson*¹, L. Green-Snyder¹, R. P. Goin-Kochel², F. K. Miller¹, J. E. Olson¹, K. Porche¹, A. V. Snow¹ and R. Bernier³, (1)*Boston Children's Hospital*, (2)*Baylor College of Medicine*, (3)*University of Washington*

Background:

Twin and family studies suggest that genetic and/or epigenetic factors are important in the development of ASD, although it is also clear that these influences are complex. Much past work in this field has been marred by inconsistent diagnostic methodology and poorly defined subject populations, which make it challenging to link particular genes to clinical subtypes.

The 16p11.2 deletion is the most common genetic disorder associated with ASD. While the exact incidence of ASD in individuals with 16p11.2 deletion is unknown, ASD and ASD-like features appear to be more prevalent in these individuals than in the general population (Fernandez et al.

2011, Hanson et al. 2010, Bijlsma et al. 2009). Medical issues also have been reported to be higher than the general population (Shen et al. 2010, Shimojima et al. 2009). In addition, there have been reports of neurological findings in these individuals (Horev et al. 2011). The Simons VIP is continuing to build an understanding of the phenotype of this disorder by investigating over 100 individuals with this recurrent genetic disorder.

Objectives: To expand the characterization of 16p11.2 deletion syndrome.

Methods: Subjects are recruited from across the United States through the Simons VIP Connect website, and travel to the clinical sites for a 2-3 day research visit. All consenting participants with a documented deletion in 16p11.2 receive a comprehensive diagnostic assessment including an Autism Diagnostic Observation Schedule (ADOS), a Diagnostic Interview Schedule for Children (DISC), cognitive, language, behavioral and adaptive skills assessments. The Autism Diagnostic Interview – Revised (ADI-R) is administered when appropriate. Comprehensive medical history information is obtained from participant report, and is also extracted from medical records.

Results: To date, we have enrolled 67 individuals (from 63 families) with a 16p11.2 deletion, all of whom are included in this interim analysis.

Within the deletion sample, 38 probands (56.7%) were male. Probands ranged in age from 20 months to 16 years, and had a mean IQ of 83.2 (SD = 16.5). Fourteen (21%) individuals received a research diagnosis of an ASD. There appeared to be an emerging pattern on ADOS scores for some individuals without ASD to have difficulties with communication and stereotyped behaviors, but not with social skills.

The most common diagnoses were Developmental Coordination Disorder (n = 35), Phonological Disorder (n = 33), Language Disorders (n = 32), and ADHD (n = 15). There were also a number of individuals diagnosed with Intellectual Disability (n = 13), Enuresis (n = 13), Borderline Intellectual Functioning (n = 13), and Disruptive Behavior/ODD (n = 9). Only 1 individual received

no diagnosis at all. Additional analyses will be conducted to look at specific symptom profiles and compare those profiles to individuals in the Simons Simplex Collection.

Conclusions: Among individuals with a 16p11.2 deletion, co-morbid diagnoses were extremely common, with 66 (98.5%) participants receiving one or more diagnoses in addition to 16p11.2 deletion. The majority of individuals have a language delay, motor deficits, and attention issues. ASD diagnosis was significantly higher than in the general population.

127.072 72 The Autism Sequencing Consortium: Prospective Genetic Data Sharing in Autism Spectrum Disorders. J. D. Buxbaum^{*1}, M. J. Daly², B. Devlin³, T. Lehner⁴, M. W. State⁵ and A. Autism Sequencing Consortium⁶, (1)*Mount Sinai School of Medicine*, (2)*Broad Institute*, (3)*University of Pittsburgh*, (4)*National Institute of Mental Health*, (5)*Yale University School of Medicine*, (6)*Mount Sinai School of Medicine, New York, NY*

Background:

There has been enormous progress in our understanding of the genomic architecture of autism spectrum disorders (ASD), which we now know to include rare variation of major effect, that can be inherited or de novo in the patient, as well as common variation of very weak effect. Based on this genomic architecture, joint analysis of thousands of samples is an efficient approach to gene discovery. Moreover, analyzing such large samples with a diverse set of approaches (for example focusing on de novo or recessive variation) would be an important means to rapidly identify ASD genes.

Objectives:

The Autism Sequencing Consortium (ASC), which includes over 20 groups working on whole exome and whole genome sequencing in ASD, is designed to analyze prospectively shared data for ASD gene discovery.

Methods:

The ASC developed a Memorandum of Understanding (MOU) for prospective data sharing that protects the contributing sites. In addition, the ASC developed Working Groups around: (1)

Data Management and Processing (DMAP), (2) Statistical Analysis (SA), and, (3) Sequencing, with standing committees around (4) Samples and Phenotypes, and (5) Production and Deliverables. DMAP developed the ASC Bioinformatic Hub where all data resides and is analyzed to ensure that all analytical approaches are defined. We collect lists of individuals and sequence data from ASC data collection centers. Centers contribute raw sequence data (FASTQ) or aligned read files (BAM). For each sample we provide a FASTQ and a BAM file; for each dataset we provide a PED file, and list of called SNPs and indels in a variant file.

Results:

The ASC MOU was signed by all members. As of October 2012, 2600 exomes are on the Hub, with another 1200 exomes being uploaded now. The data consumes 81 terabytes of storage. Based on the exome sequencing studies going on to date, we expect to have over 20,000 exomes available for analysis within 3 years. A Variant Calling Subgroup produces optimal calls of the exomes for single nucleotide variation, indel, and, ultimately copy number variation (CNV). The SA working group is developing analytical approaches to the whole exome data.

Conclusions:

Prospective data sharing is a means to rapidly identify ASD genes and accelerate research in the pathogenesis and treatment of ASD.

127.073 73 ASD Associated Promoter Variants in the CNTNAP2 Gene Modulate Gene-Expression and Language Development. M. Kopp¹, A. Chiocchetti*¹, E. Duketis¹, A. Voran², U. Graab¹, J. Meyer³, S. M. Klauck⁴, S. Fulda¹ and C. M. Freitag⁵, (1)Goethe-University, (2)Saarland University, (3)University of Trier, (4)German Cancer Research Center (DKFZ), (5)Goethe University

Background: Autism spectrum disorders (ASD) are mostly genetically determined and marked by aberrant social and reciprocal communication, language development and behavior. Recurrent findings have suggested variants within the *CNTNAP2* gene as risk factors for ASD especially associated with delayed language development. Although CNVs within the relevant gene region reported for individuals with ASD reduce *CNTNAP2*

expression levels, studies so far have not focused on the promoter region, i.e. the regulator for gene expression.

Objectives: In this work we investigated if *CNTNAP2* promoter variants are associated with ASD. Furthermore we characterized their functional impact on the transcriptional efficiency.

Methods: Direct sequencing of the *CNTNAP2* promoter region was performed on a detection sample of 247 families with ASD. Variants with a genotype frequency > 1% were genotyped using RFLP in additional 356 families. Transmission disequilibrium testing was performed by UNPHASED. Impacts on transcriptional efficiency were investigated applying a luciferase-reporter gene assay.

Results: In our detection sample we identified three annotated variants with a genotype frequency over 1% (rs150447075, rs34712024 and rs71781329) and six undescribed variants in single subjects. A preliminary family-based association study of the three annotated SNPs showed a significant association for rs34712024 (OR=0.200; CI95=0.044-0.913; p=0.0158) and rs71781329 (OR=inf.; CI95=inf.; p=0.0177), respectively. The power was too low to replicate the finding in the additional set and we thus combined the two samples and identified a significant association for rs34712024 (OR=0.409; CI95=0.1884-0.884; p=0.0177). Luciferase assay tests showed that all three variants significantly increased transcriptional efficiency. Prediction of transcription factor binding sites suggested that rs150447075 and rs34712024 lie within the binding region of the transcriptional repressor NRSF. The trimeric insertion rs71781329 is predicted to generate an additional TF binding site for EGR1, explaining increased transcription.

Conclusions: Given the findings that i) the variants analyzed here increased the transcriptional efficiency and may thus lead to an elevated level of *CNTNAP2* and ii) the OR for the minor allele of rs34712024 is smaller than 1, it can be assumed that increased *CNTNAP2* expression is protective for ASD. This is supported by the finding in a CNV study that a decreased *CNTNAP2* expression may contribute to the risk for ASD. In conclusion, we could show that

CNTNAP2 promoter variants play a crucial role in the ASD etiology. *CNTNAP2* provides an important factor to be functionally characterized to better understand ASD related biological processes.

127.074 74 X-Linked Imprinted Genes and Sex-Ratio Bias in Autistic Spectrum Disorders. M. J. O'Neill*, *University of Connecticut*

Background: Two prevailing theories attempt to explain the strong male bias in the occurrence of Autistic Spectrum Disorders (ASD). Baron-Cohen has proposed that the male prevalence can be ascribed to fetal exposure to testosterone, which may masculinize developing neural circuitry exacerbating an underlying predisposition to an "extreme male brain". Contrarily, Skuse has hypothesized that the male prevalence to ASD can be attributed to hemizyosity of the X chromosome in boys, exposing them to perturbations in gene dosage brought about by X chromosome epigenetic phenomena. Despite their prominent treatment in the literature over the past decade, neither theory has gained much traction due to a lack of general and compelling physiological data supporting the former and genetic or epigenetic data supporting the latter.

Objectives: We hypothesize that the male bias in ASD may be attributable to the influence of parent-of-origin expression (i.e. imprinting) of X-linked genes. Since males receive only the maternal X chromosome, the true effect is one of "grandparent-of-origin". In other words, the single X in males is a mosaic of alleles passed from either the maternal grandmother or maternal grandfather. Epigenetic signatures that are disrupted in the grandparents, or are improperly established or reset in the mother may be passed to her sons. While transgenerational effects of parental or grandparental age in ASD susceptibility have been investigated, a genome-wide or candidate gene approach has not been attempted.

Methods: In a candidate gene approach to identify X-linked imprinted genes we are employing whole transcriptome analysis via microarray and RNA-seq on brain RNA from X monosomic mouse models. It is clear that current GWAS have underutilized data available for the X chromosome. In a genome-wide association approach we are testing for statistical correlation between maternal grandparental X chromosome

SNP profile and incidence of ASD in males utilizing novel analytical tools.

Results: We have identified an X-linked gene that exhibits parentally biased expression: *Transketolase-like 1 (Tktl1)*. *Tktl1* exhibits region-specific transcriptional repression of the paternal allele in neonatal mouse brain. *TKTL1* maps to the syntenic region (Xq28) of the human X and we have recently confirmed imprinted expression of this gene in human fetal brain tissue. Our genome-wide approach to uncover transgenerational X-linked effects is ongoing.

Conclusions: *TKTL1* encodes a transketolase enzyme that constitutes a rate-limiting step in the bifurcated pentose phosphate pathway (PPP) of glycolysis. The cyclic portion of the PPP is the primary pathway for the production of NADPH, which is necessary for the maintenance of redox potential in cells, protecting them from oxidative damage. Numerous studies in the last several years have established a link between oxidative stress and autism. Our work supports the hypothesis that the male bias in ASD occurrence may be attributable to X chromosome epimutation.

127.075 75 Exome Sequencing of a Multiplex Family with Autistic Spectrum Disorder. B. Tawil¹, A. H. Adi¹, M. Aldosari², M. Nester¹, H. M. ALDhalaan¹, E. Naim¹, D. Monies¹, M. Ghannam³, B. F. Meyer¹ and N. Al Tassan^{*1}, (1)*King Faisal Specialist Hospital and Research Center*, (2)*Mercy Pediatric Neurology and Psychiatry Center*, (3)*King Faisal Specialist Hospital & Research Centre*

Background:

Autistic Spectrum Disorders (ASD) represents a genetically complex developmental disorder. Several approaches have been used to find candidate genes linked to/ or associated with ASD. These include genome wide scans, linkage studies of multiplex families, cytogenetic studies and copy number variation [CNV]. These different approaches have yielded a number of associated and susceptible genes and high risk loci. Single base pair substitutions in *NLGN3*, *NLGN4* and *SHANK3* genes were identified in rare cases of ASD with different degrees of severity.

Objectives:

Utilize next generation sequencing (exome sequencing) in highly inbred families with three or more affected members to identify variants associated with ASD.

Methods:

This is a report of one of the families from an approved collaborative research project of multiplex ASD families in Saudi Arabia. Large, highly inbred families with more than three affected members were enrolled after exclusion of the known genetic and metabolic etiologies. Exome sequencing was performed in one affected individual, variants identified were selected based on predicted pathogenicity and screened in all family members for validation and segregation.

Results:

Whole exome sequencing identified 23 potential pathogenic novel variants in 20 genes. These variants were screened in all family members. Only 2 changes noted in the gene *HNRNPK*, Exon 9 in which there was a heterozygous insertion (INS c.641[-/T]) and another heterozygous deletion (DEL c. 519-93 [G/-]), and a missense variant T129I (c.386 C>T) in *ERCC8* segregated with the disease in family members.

Conclusions:

The current report supports the heterogeneity of the genetic basis of ASD and the possible interaction of more than one gene on different chromosomes in the same family.

127.076 76 Testing the Molecular Genetic Basis of Transmission of Autism Risk by Healthy Mothers. J. Dougherty*¹, H. Yuan¹ and J. N. Constantino², (1)*Washington University*, (2)*Washington University School of Medicine*

Background: Sibling and family studies from our laboratory have strongly suggested that a substantial proportion of all cases of autism spectrum disorders occur on the basis of susceptibilities inherited from unaffected, or sub clinically affected parents, and that the universally-observed gender ratio in autism may, in part, be attributable to asymptomatic carriage of inherited liability in females.

Objectives: Here, we examine two previously-unexplored models for the molecular genetic basis of this hypothesized phenomenon: the first to determine whether there exist systematic differences in common variant profiles of mothers of children with autism in known autism risk alleles; the second to identify a possible contribution of maternal genotype to environmental susceptibilities of their offspring.

Methods: These models are tested both utilizing genetic epidemiological approaches employing the IAN registry, as well as analysis of data from the Simons Simplex Collection(SSC) and Autism Genetic Research Exchange (AGRE). Parents of probands were selected from AGRE dataset, and individuals genotyped from the same platform were collected from iControlDB. Principal components analysis was done to identify population substructure using smartpca. Components were taken as covariates in eventual association tests to correct for population substructure. After data cleaning, we obtained 561 AGRE mothers, 547 AGRE fathers, 508 iControl females, and 547 iControl males. To identify alleles present specifically in mothers that may be contributing to autism risk in their offspring, we compared AGRE mothers to AGRE fathers as well as to iControl females. A two-way association analysis was done using PLINK based on the logistic model, with the assumption non-spurious results should be nominally significant in both comparisons. For replication, we repeated the same analysis using the SSC collection and independent controls.

Results: Within our power to detect differences in this initial exploration (OR>2.5), we did not discover polymorphisms that reached genome-wide significance in the mothers of children with autism. However, we identified 14 SNPs with p-value<10E-6 (compared to 8 expected by chance), suggesting alleles in the mothers' genomes that may make a contribution to autism risk. None of the regions identified from previous common variant studies of autism were among our top candidates, indicating that if these eventually replicate they might index specific maternal genetic contribution to environmental risk.

Conclusions: This initial approach was not able to specify the molecular genetic variations

underlying asymptomatic transmission of autism risk, and it is highly likely that larger samples will be required to elucidate these factors. This method for investigating family-based data formaternal and paternal genetic contribution to risk can be systematically applied to other available data sets, and with the evolution of larger-sample-size data repositories can be equally applied to studies of rare inherited variants influencing autism risk within families.

127.077 77 The Role of Chromosome X in ASD Sex Bias. J.

Gockley*¹, A. J. Willsey¹, J. N. Constantino², S. J. Sanders¹ and M. W. State¹, (1)*Yale University School of Medicine*, (2)*Washington University School of Medicine*

Background: ASD is observed at a higher rate in males than females (4:1); a simple explanation for this bias is X-linked risk variants in the male. While Fragile X (*FMRP*) is the most common cause of ASD there are few ASD families that display clear X-linked inheritance leading to gene discovery (with the exception of *NLGN4X*). Alternative mechanisms of sex bias include female protection by virtue of the diploid chromosome X (chrX) or an excess of chrX-based common inherited risk variants. Analysis of the distribution of Social Responsiveness Scale (SRS) scores in 515 female individuals from multiplex families of the AGRE collection showed a bimodal distribution not found in males. This raises the possibility that a common allele leads to higher sociability and therefore ASD protection but only in the diploid homozygous state (i.e. not in males or subset of females). To account for a sex bias of 4:1 the variant would require a minor allele frequency of 14% and to be present on a region of chrX that escapes X-inactivation and has no homologue on chrY.

Objectives: To identify if a common variant on chrX leading to ASD protection is present in an identified subset of females with ASD.

Methods: 261 unaffected and 254 affected females from the AGRE sample set were used for initial discovery. Both sample groups were split into high and low SRS score subsets (divided by an SRS score of 45 and 87 in the unaffected and affected groups respectively). Principle component analysis was used to select only individuals of European ancestry. Standard genotype data cleaning procedures were used including genotyping call rate >99%, Hardy Weinberg

Equilibrium (p-value <0.05), and SNP call rate >90%. Only SNPs within regions shown to escape X-inactivation, as defined by Carrel and Willard 2005, and outside of the pseudo-autosomal regions and X-transposed region were considered for analysis. Analysis was restricted to SNPs with a minor allele frequency of 14% ±10% in line with the hypothesis. A replication set comprising 710 unaffected females, similarly classified into higher and lower SRS scoring subsets, and 244 affected females was used.

Results: We found a single SNP (rs5936079) at Xp22.2 that approached significance with a Bonferroni corrected p-value fractionally greater than 0.05 in the discovery set for the comparison of high SRS scoring unaffected females versus low SRS scoring affected females. The minor allele was C with a frequency of 20%; odds ratio was 4.76 (95% CI: 2.22-10.0). In the SSC replication set this same SNP had a p-value of 0.42 in high SRS scoring unaffected females versus all affected females (regardless of SRS).

Conclusions: No SNP was identified matching our hypothesis after correction for multiple comparisons in either the discovery or replication set. However the top scoring SNP was observed at the frequency predicted by the hypothesis and merits follow up in a larger sample set. Our method of pursuing specific association hypotheses based on predicted allelic characteristics represents a novel approach to investigating biological phenomena in genotyping data.

127.078 78 Targeted Massively Parallel Sequencing of GWAS

Association Peaks in a Case and Control Cohort Identifies Rare Autism Spectrum Disorder Risk Variants. J. Gilbert*¹, A. J. Griswold¹, D. J. Hedges², R. H. Chung¹, J. A. Rantus¹, P. Whitehead¹, I. Konidari¹, W. Hulme¹, S. H. Slifer¹, J. Jaworski¹, S. M. Williams³, R. Menon⁴, M. L. Cuccaro⁵, E. R. Martin⁵, J. L. Haines⁶, J. P. Hussman⁷ and M. A. Pericak-Vance⁵, (1)*University of Miami*, (2)*The Ohio State University*, (3)*Dartmouth College*, (4)*University of Texas Medical Branch*, (5)*University of Miami Miller School of Medicine*, (6)*Vanderbilt University*, (7)*Hussman Foundation*

Background: Genome-wide association studies (GWAS), copy number variation screens, and candidate gene studies have found no single factor accounting for a large percentage of genetic risk for autism spectrum disorders (ASD). This has led to the hypothesis that many genetic variants

in potentially hundreds of genes contribute to ASD. To identify these rare risk variants sequencing of large datasets for rare or low frequency variants with potential functional significance to ASDs is essential.

Objectives: To identify new variants contributing to ASD risk by sequencing ASD candidate genes and GWAS associated regions in a large dataset.

Methods: Candidate regions were chosen from GWAS Noise Reduction analyses of two autism datasets with prioritization of haplotype blocks based on the Truncated Product Method (TPM) (Hussman et. al., 2011). We designed an Agilent SureSelect probe set covering 17Mb corresponding to: 1) exons of 681 genes overlapping blocks with TPM p-values<0.05; 2) evolutionarily conserved regions in those genes plus 5kb from their transcriptional starts and ends; 3) evolutionarily conserved regions within non-genic blocks with TPM p-values<0.05; and 4) entire blocks with TPM p-values<0.01. Illumina HiSeq2000 reads were processed with the Burrows-Wheeler Aligner, genotypes called with the GATK Universal Genotype Caller, and annotated with SeattleSeq134, PolyPhen2, and SIFT. We have completed analysis of 951 unrelated ASD cases and 872 controls. Among these, Eigenstrat stratification identified 598 white cases and 433 controls for further analyses. Gene-based association testing between targeted genes and ASD was performed with the Sequence Kernel Association Test (SKAT) utilizing a regression approach adjusting for covariates. A follow-up validation study of an additional 2000 individuals is underway.

Results: In the dataset, $87.9 \pm 6.3\%$ of targeted bases are covered at least 10X with an average on target depth coverage of $78.1 \pm 25.9X$. A total of 231,945 single nucleotide variants (SNVs) pass quality controls with a call rate of at least 99% across all samples. Of these, 21,263 SNVs are exonic, 6,512 are non-synonymous changes, and 4,028 are predicted to adversely affect protein function. We examined 69 genes that had been previously implicated in ASD. These contain 47,111 SNVs: 3,579 exonic, 1,118 non-synonymous, and 656 damaging. Of the damaging variants, 307 are unique to cases and several are in established ASD genes including 10 SNVs in *CNTNAP2*, 7 in *MACROD2*, 4 in *NRXN1*,

and 5 in *SEMA5A*. Moreover, we found 47 genes in which only cases have more than one rare (MAF<0.01) damaging alteration in a single individual, including the autism candidates, *CNTN3*, *CDH8*, *IL1RAPL2*, and *PSD3*. Rare variant association testing with SKAT identified nominally significant association of sets of rare exonic variants (p<0.05) with ASD in 16 genes including the voltage dependent calcium channel *CACNA2D1* (p=0.00079) and the intracellular transport regulators *GNPTAB* (p=0.0049) and *BICD1* (p=0.01).

Conclusions: These studies yield important findings regarding rare, potentially functional, SNVs found uniquely in ASD cases in previously identified and new candidate genes establishing targeted sequencing of ASD candidate genes/regions as a powerful method for discovery of new genetic variants contributing to ASD risk.

127.079 79 Molecular Phenotypes Associated with Total Cerebral Volume in Boys with Autism Spectrum Disorders. B. S. Stamova*¹, Y. Tian¹, C. W. Nordahl², M. D. Shen³, S. J. Rogers³, D. G. Amaral³ and F. R. Sharp¹, (1)University of California Davis Medical Center; MIND Institute, (2)University of California Davis Medical Center, (3)MIND Institute; University of California at Davis

Background: We recently described molecular pathways affected by differential exon usage (DEU) / and differential alternative splicing (DAS) that were common to a number of ASD boys. In this study we investigated the divergent molecular pathways in blood associated with different total cerebral volume (TCV) phenotypes of boys with ASD. Megalencephaly is an endophenotype present in about 11-15% of subjects with ASD that has been associated with regression status. We postulated that the genetic and/or environmental factors that cause differences of TCV would affect DEU/DAS in blood and contribute to our understanding of the molecular differences associated with these ASD subgroups.

Objectives: We aimed to identify differences in predicted DAS/DEU in blood cells of 2-4 year old ASD boys with large TCV (LTCV) and normal TCV (NTCV) compared to age-matched typically developing (TD) boys.

Methods: Subjects were recruited through the Autism Phenome Project (M.I.N.D. Institute). The study included 20 ASD boys with NTCV (3.0 ± 0.5

years), 10 ASD boys with LTCV (3.1 ± 0.2 years), and 20 TD boys (3.0 ± 0.3 years). Brain MRI defined the subgroups, with the LTCV group having a mean TCV of 1.5 standard deviations greater than the average TCV of matched TD controls. Predicted DAS/DEU was assayed using whole blood on Affymetrix exon arrays. A two-level analysis defined the most reliable set of genes predicted to have DAS/DEU (Partek). First, an Alternative Splicing ANCOVA was performed on Group, with Covariates for both technical (Batch, random effect) and biological (Age, continuous variable) variation. Genes with DAS $p < 0.05$ were considered significant. Second, an exon-level expression ANCOVA on Group, with age and batch as co-variates, was performed. Exons with $p < 0.005$ and $|\text{Fold-Change}| > 1.2$ on each Group comparison were considered significant. The genes common to both analyses were considered to be the most reliable because they were predicted to display DAS and to have significant differences of exon-level expression.

Results: 764 genes are predicted to exhibit DAS/DEU in ASD_NTCV vs TD, 23 of which overlapped with genes implicated in ASD (SFARI database, 369 genes, p of overlap=0.07). The 764 genes were over-represented in Dendritic Cell Maturation, NF-kappaB, Actin Cytoskeleton, and Ephrin A (Axon Guidance). 16 of the 764 genes overlapped with the 211 genes reported by Voineagu *et al.* (Nature, 2011) as having DAS in ASD brain (overlap $p=0.01$). 212 of the 764 genes pass FDR < 0.1 for DAS. A different molecular signature was associated with ASD boys with LTCV when compared to TD controls with 124 genes predicted to exhibit DAS/DEU. They were over represented in 5-amidoimidazole Ribonucleotide Biosynthesis I (Nucleotide Biosynthesis), Palmitate Biosynthesis I (Fatty Acid Biosynthesis), Netrin (Axon Guidance /Nervous System Signaling), Leukocyte Extravasation (Cellular Immune Response), and Tetrahydrofolate Salvage from 5,10-methenyltetrahydrofolate (Folate Biosynthesis) signaling pathways. 14 genes overlapped the two comparisons.

Conclusions: We provide evidence for DAS/DEU in blood associated with different TCV in 2-4 year old boys with ASD. The data suggest that differences of TCV in boys with ASD are associated with specific molecular pathways and a specific

pathophysiology. RNA-Seq analysis is underway to validate findings.

127.080 80 Evidence of a Maternally Acting Gene Allele (MAGA) for Autism in a Second Dataset in a Small Region of Chromosome 3p24.3. W. G. Johnson^{*1}, E. S. Stenroos¹ and S. Buyske², (1)UMDNJ-RWJMS, (2)Rutgers University

Background: Maternally-acting gene alleles, MAGAs, act in mothers prenatally to alter fetal environment and affect offspring phenotype, independently of any inheritance by the fetus. We have also used the terms "maternally acting alleles" and "teratogenic alleles" for these. There have been over 70 reports of MAGAs to date, mostly in neurodevelopmental disorders. Six of these reports were in autism. Evidence of MAGAs has previously been found by candidate gene approaches. Earlier, we reported the first, to our knowledge, genome-wide association study (GWAS) for MAGAs that implicated a small region of chromosome 3p24.3 for autism using existing data from 825 families in the Autism Genetic Resource Exchange (AGRE) studied on the Illumina Hap550 GWAS array. SNP rs12487874 (intronic in the *RTFN1* gene) showed genome-wide significance ($p=8.61E-11$) with no evidence of child effect (presented at IMFAR 2012).

Objectives: To replicate our preliminary findings with a second dataset.

Methods: We used the Weinberg log-linear method to analyze existing GWAS data from 1366 families in the Autism Genome Project (AGP) genotyped on the Illumina 1M array.

Results: The AGP dataset showed genome-wide significance ($p = 1.83E-19$) for SNP rs12636481, located near rs12487874 and not in the earlier dataset. SNP rs12487874 was not part of the AGP dataset. Both SNPs showed a marked asymmetry in parents in both studies, where the mothers identified were homozygotes for the minor allele.

Conclusions: Since this study confirmed a peak for autism in a small region of chromosome 3p24.3, we plan to analyze data from a much larger dataset, the Simons Simplex Collection (SSC), to confirm and extend these findings. We will also re-genotype the SNPs identified using a more stringent method to confirm these findings and to exclude possible artifacts. If these findings are

confirmed by analysis in the SSC and re-genotyping, we will then test the hypothesis that a structural DNA variant in this region is responsible for the observed effect. These studies could lead to identification of DNA variation in this region 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.

127.081 81 The DRD3 Gene and Striatum in Autism Spectrum Disorder (ASD). W. Staal^{*1}, M. Langen², S. C. V. Dijk³ and S. Durston², (1)*Radboud University*, (2)*Rudolf Magnus Institute of Neuroscience, University Medical Center Utrecht*, (3)*UMC Utrecht department of Psychiatry*

Background: Recently the SNP rs167771 (DRD3) was found to be associated with ASD in two independent samples. Further exploration showed that rs167771 polymorphisms correspond to different levels of higher order stereotyped behaviour in ASD (Staal, 2012).

Objectives: Since the DRD3 receptor is also highly expressed in the striatum, we tested the hypothesis that changes in striatum were related to polymorphisms of rs167771 in autism.

Methods: To test this hypothesis, the volume of striatum (caudate, putamen, gl pallidus) and the whole brain were measured using freesurfer on anatomical MRI scans from 86 subjects with ASD. Behavioural assessment included the ADI-R, ADOS, IQ assessment and genotyping of rs167771.

Results: MANCOVA showed a significant association between the rs167771 minor allele and striatum volume ($F= 2.582$ ($df= 4$); $p=.046$). In an explorative follow up analysis, the volume of striatum correlated with higher order stereotype behaviour ($R=.278$; $p=.040$).

Conclusions: These data suggest that there may be a relationship between a common variant of the DRD3 receptor gene, striatum volume and stereotyped behaviour in ASD. If this preliminary result replicates, future studies will need to address whether the observed relationships are

specific to ASD or whether they represent a broader biological mechanism.

References: Staal WG, de Krom M, de Jonge MV. Brief Report: The Dopamine-3-Receptor Gene (DRD3) is associated with Specific Repetitive Behavior in Autism Spectrum Disorder (ASD). *J Autism Dev Disord.* 2012 May;42(5): 885-8.

127.082 82 Identifying Underlying Disease Mechanisms in Autism Using iPSC-Based Models of Neurodevelopment. D. M. Dykxhoorn*, B. A. DeRosa, J. M. Van Baaren, J. M. Lee, M. L. Cuccaro, J. M. Vance and M. A. Pericak-Vance, *University of Miami Miller School of Medicine*

Background: Autism spectrum disorder (ASD) is a heterogeneous, neurodevelopmental disorder characterized by deficiencies in social interaction, verbal and non-verbal communication, and repetitive stereotypical behaviors. Although advances have been made in our understanding ASD pathophysiology, many questions still remain. A major constraint in ASD research has been the paucity of disease-relevant tissues and cells with which to study the molecular mechanisms of ASD. A number of studies have used post-mortem brain tissue collected from individuals affected with autism. However, any findings that are identified in post-mortem ASD brain samples are likely to only represent an end point in the pathology of autism. Since ASD is a neurodevelopmental disorder, approaches are needed that will facilitate analysis during neurogenesis.

Objectives: The focus of this work was to examine the molecular mechanisms that underlie the cellular pathophysiology of ASD during neurodevelopment using patient-specific induced pluripotent stem cells (iPSCs) as a model. This method permits the observation 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, thus represent potentially vulnerable cell populations in this neurodevelopmental disorder. 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) derived from individuals with autism and healthy control individuals. These iPSC lines were validated for their pluripotency and self-renewal characteristics by immunocytochemical staining and quantitative real-time PCR analysis of key pluripotency genes. Once validated, the ASD-specific and control iPSC lines were differentiated into GABAergic or glutamatergic neurons through the serial treatment with cytokines and morphogens aimed at inducing neurogenesis and mimicking the *in vivo* temporal process. The mature, fully differentiated neurons were functionally characterized for electrophysiological activity, morphology and synapse formation.

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 in a process that imitates *in vivo* neurodevelopment. Neurons derived from the ASD-specific iPSCs exhibit aberrations in cellular function and structure compared to iPSC-derived neurons from unaffected individuals. This system provides an ideal opportunity for the application of high content transcriptome analysis and functional characterization to illuminate the fundamental biological processes at play in the development of autism. This strategy has proved useful at answering important questions about the pathophysiology of autism involving excitatory/inhibitory balance and could potentially be used toward the advancement of novel therapeutics and the identification of biomarkers to improve diagnosis for early intervention.

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.

127.083 83 Maternal Interstitial 15q-11q13 Duplication Is Sufficient to Produce and Autism Phenotype. N. Urraca*, *UTHSC*

Background: Chromosomal copy number variants (CNV) are the most common genetic lesion found in autism. As many as 3% of autistic cases may be the result of duplications of chromosome 15q. The 15q11-q13 region has a cluster of genes preferentially expressed from one parental allele. Most 15q duplication cases that present clinically

are maternally derived and *de novo*, although paternal cases have also been identified. There are two main classes of deletion/duplication in this region: class I CNVs with breakpoints from BP1 to BP3 and class II CNVs with breakpoints from BP2 to BP3.

Objectives: The aim of the present study was to determine if maternal duplication is sufficient for the diagnosis of autism spectrum disorder and characterize differentiating symptomatology between maternal Class I and Class II subjects.

Methods: Subjects were recruited through the 15q Alliance parent support group (www.dup15qalliance.net). We used neuropsychological and ASD diagnostic tools for phenotypic analysis. Methylation Sensitive High Resolution Melting (MS-HRM) analysis of the maternally methylated *SNRPN* locus was used to determine the parent of origin of the duplication.

Results: Fifteen subjects were recruited. Twelve were *de novo* and 3 inherited cases. MS-HRM Indicated 11 maternal and 4 paternally derived or inherited cases. All maternal subjects tested (10) with ADOS/ADI-R scored in the autism spectrum, while just half of paternal duplication cases were autistic. There is no significant difference in the ADOS, ADI-R and SRS parameters between maternal class I and class II subjects. IQ testing in 6 subjects with maternal duplication indicated only mild intellectual disability (76.8 ± 9.3). The 10 maternal autistic subjects in the study had a low-moderate adaptive functioning score in all Vineland scales with no differences among groups. There was a negative correlation between ADOS severity and the Vineland II scores but it was not significant.

Conclusions: Our results suggest that a maternally expressed gene, most likely *UBE3A*, is primarily responsible for the autism phenotype in interstitial duplication 15q cases since all maternal duplication cases presented on the autism spectrum. The size of these duplications did not correlate with autism severity and symptomatology

127.084 84 Is Sensory Responsiveness an Endophenotype of Autism Spectrum Disorders?. C. L. Hilton*¹ and C. L. Kloth²,
(1)Washington University, (2)Washington University School of Medicine

Background: For children with autism spectrum disorders (ASD), atypical sensory responsiveness has been shown to be much more common than among children unaffected with ASD. Although numerous studies have examined the social abilities of siblings of children with ASD, few have examined their sensory characteristics. An aggregation of sub clinical autistic social impairment traits and complex immune dysfunction have been found in unaffected family members of children with ASD, suggesting that such impairments constitute autism endophenotypes (traits that are associated with a diagnosis, are heritable, and manifest in family members with or without the diagnosis). It is important to determine if patterns of atypical sensory processing occur in unaffected members of ASD families to better understand the heritability of this trait and the vulnerability of siblings for sensory responsiveness issues.

Objectives: This study examined the sensory responsiveness of children with ASD and controls, including sibling pairs in children from families with ASD, to better understand the heritability of atypical sensory responsiveness in families with ASD. In addition, differences in sensory responsiveness patterns were examined across ages from 4 to 17.99 years in children with and without an ASD diagnosis.

Methods: Sensory Profile Caregiver Questionnaires (SPCQ; for < age 11) or Adolescent and Adult Sensory Profile Questionnaires (AASP; for age 11+) were completed by parents of 253 children between age 4 and 17.99 (158 ASD, 54 unaffected siblings and 41 controls; 209 white, 42 black, 2 Asian). Common sensory responsiveness items for the four sensory quadrants (overall patterns of responses: low registration, sensation seeking, sensory sensitivity, sensation avoiding) and five sensory domains (responses to specific types of sensory input: auditory, visual, touch, vestibular, taste/smell) were analyzed. Use of the common items allowed for inclusion of participants from both Sensory Profile age categories and raw quadrant and domain scores were compared between probands, affected siblings, unaffected siblings and controls. Common item scores were also compared across ages for affected and unaffected children.

Results: Significant differences were seen in scores between children with ASD and their unaffected siblings for all sensory domains and quadrants. Significant differences were seen in scores for the vestibular domain ($p=.02$) and the sensation avoiding quadrant ($p=.008$) between unaffected controls and unaffected siblings. No differences were seen between Caucasian and African American children.

Patterns of significantly more typical responses were seen in unaffected children as their ages increased from 4 to 17.99 years in three of the four quadrants. For the children with ASD, close to significance was seen as the ages of the children increased in two of the four quadrants. Scores showed similar patterns of significantly more typical responses in unaffected children but not in the children with ASD in visual, vestibular, auditory and gustatory/olfactory, but not tactile domains with increased age.

Conclusions: Findings suggest that some degree of heritability in the sensory responsiveness is present among siblings from the families affected with ASD. In addition, trends toward more typical sensory responsiveness are generally seen in older typically developing children, but rarely in children with ASD.

127.085 85 Multiple Rare Genetic Variants Can Deregulate Common Pathways in Autism Spectrum Disorders. I. Cusco^{*1}, B. Rodríguez-Santiago², J. Santoyo-Lopez³, M. Rigau⁴, G. Aznar Lain⁵, M. Codina¹, A. Homs⁴, A. Gutiérrez⁶ and L. A. Pérez-Jurado¹, (1)*Instituto de Investigación Sanitaria IMIM-Hospital del Mar*, (2)*Quantitative Genomic Medicine Laboratories, S.L. (qGenomics)*, (3)*Medical Genome Project (MGP)*, (4)*Universitat Pompeu Fabra*, (5)*Servei de Pediatria, Hospital del Mar-Parc de Salut Mar*, (6)*The Centre for Biomedical Network Research on Rare Diseases (CIBERER)*

Background: Autism spectrum disorders (ASD) are a group of neurodevelopmental disorders with an increasing reported incidence over the past decade. There is strong evidence for a genetic etiology of ASD (90% of concordance rates in monozygotic twins) but it is thought to be a complex multifactorial disorder with several loci involved. Recent genetic findings using molecular karyotyping and next-generation sequencing support a possible double or multiple-hit model for ASD that could explain the heterogeneity in ASD.

Objectives: Under the assumption that the genetic source of ASD phenotype is mainly the multiple-hit model, we try to identify both causative genes (*de novo* variants) and common altered pathways affected as a consequence of the multiple rare genetic variants (inherited variants).

Methods: We have analyzed 30 idiopathic male ASD cases (DSM-IV and ADI-R evaluation) using the exome sequence approximation. We have only considered the rare genetic variants (indels and SNV) with theoretical severe functional implications (stop, non-synonymous and frame-shift mutations) under the dominant (private heterozygous variants), recessive (homozygous or compound heterozygous) and X-linked models. We have used Sanger sequencing and Sequenom technology for validation and co-segregation studies. Pathways enrichment studies were performed using the free available resource ConsensusPathDB (<http://cpdb.molgen.mpg.de>).

Results: We have detected some likely causative mutations with monogenic mendelian models in three cases: one *de novo* stop mutation in *SCN2A* and two X-linked mutations (*MAOA* and *CDKL5*). Exome data revealed on average 72.6 rare events per sample. We have detected that 4.2% of the affected genes had been previously described in relation with ASD (SFARI + AutismKb databases N=666 genes) with significant overrepresentation ($p=0.001$; $OR=1.5$). We have found 249 genes with multiple rare variants (in more than 1 ASD patient) being 11 of them strong candidates (*CREBBP*, *ERBB4*, *GRIN2A*, *SCN2A*, *ANK3*, *CLTCL1*, *EML1*, *ESR1*, *SYNE1*, *CSMD3*, *TTN*). We have detected that most of these variants are inherited from healthy parents, a fact that is consistent with an additive model rather than a sporadic event. Pathway studies have been performed individually, and we have detected common overrepresentation of 35 pathways (ex. Interaction between L1 and Ankyrins, NCAM signaling for neurite out-growth, axon guidance, Semaphorin interactions). Further investigations of overrepresented pathways detected in control sample are still in process in order to distinguish ASD specific pathways.

Conclusions: We have identified presumably causative mutations in 10% of our patients compatible with monogenic ASD. The exome data also revealed rare variants in genes previously

reported as strong candidates for ASD significantly enriched in our cohort of ASD patients. Eleven of those genes were altered in multiple samples indicating a common defect. Being most of the variants inherited our data support a multiple-hit model for ASD where the co-occurrence of several genetic variations altering common pathways are responsible for the phenotype.

127.087 87 Play in Mother-Child Interaction: Comparison Between Children with Autism Specutum Disorder, Children with Down Syndrome and Children with Typical Development. A. Bentenuto*¹, S. Riccadonna², C. Furlanello³ and P. Venuti¹, (1)University of Trento, (2)Bruno Kessler Foundation FBK, (3)FBK - Fondazione Bruno Kessler

Background: Children, during the play have the chance to develop not only motor skills but also cognitive and social skills (e.g. Bornstein, 2007). Much of children's first learning and many of their first experiences occur during play (Tamis-LeMonda & Bornstein 1996; Bornstein 2007). Caregiver involvement in child play activities enhances the frequency, the duration, and the complexity of child play both in typically developing children and in children with atypical developmental (Bornstein et al. 1996, 2002; Venuti et al. 1997, 2008). In addition, children with ASD show less spontaneous, frequent and limited symbolic play, spend less time in such play and show fewer extended sequences of symbolic play compared to typically developing children or children with intellectual disabilities (Blanc et al, 2005; Jarrold et al, 1996, Rutherford and Rogers 2003).

Objectives: The aim of the present study is to investigate the play during mother-child interaction in children with ASD compared to children with DS and typically developing (TD) mental-age-matched.

Methods:

A total of 75 children and their mothers took part. The index group consisted of 25 children with ASD (M mental age = 24.2 months, SD 9.8; M chronological age = 43.3 months, SD = 7.6) and their mothers, of 25 children with DS (M mental age = 21.1 months, SD 4.3; M chronological age = 37.7 months, SD = 8.6) and their mothers and a group of 25 mental-age-matched typically developing children (M chronological age = 20.01 months; SD = .21) Data were collected during 10-

min play-sessions. A set of standard, age-appropriate toys that represent feminine, masculine, and gender-neutral categories was used. During the session, the mother was asked to play individually with her or his child, as they typically would do. Sessions were video recorded. The play code consisted of mutually exclusive and exhaustive category system that included eight levels and a default (no play) category (see Bornstein et al., 1996;). Levels 1-4 constitute the macrocategory Exploratory play, and Levels 5-8 constitute the macrocategory Symbolic play.

Results: Considering the structure of child play, we found a general prevalence of exploratory activity in the three groups. Either groups had a mean mental age of approximately 20 months, which means they should have already achieved some symbolic play, which they had, but are still very much engaged in exploration of the environment. The SD children show less exploratory play less compared with TD children or ASD children. For the symbolic play we found ASD children presented the same level and duration as SD children or children with typical developmental.

Conclusions:

the children with ASD engaged in symbolic play similar to metal-age matched children, and this information can help to improve some interventions that use play.

127.089 89 Language Abilities and Traits of Autism Are Aetiologically Distinct: Evidence From a Community-Based Twin Study of 12-Year-Olds. M. J. Taylor*¹, T. Charman¹, E. Robinson², P. S. Dale³ and A. Ronald⁴, (1)*Institute of Education*, (2)*Analytic and Translational Genetics Unit, Massachusetts General Hospital/Department of Medicine, Harvard School of Medicine*, (3)*University of New Mexico*, (4)*Birkbeck College*

Background: Atypicalities in communication are considered to be one of the core features of autism, and often include delays in the development of spoken language. While numerous studies have explored language in autism (see Groen et al., 2008 for a review), there have been only two previous twin studies exploring the association between language and autism-related traits (e.g. Dworzynski et al., 2007, 2008).

Objectives: The present study aimed to investigate, in depth, the genetic and environmental underpinnings of the association between traits of autism and language as assessed by four different measures of language ability when twins were aged 12-years.

Methods: Parents of ~5,000 twins participating in the Twins Early Development Study (TEDS) completed questionnaires assessing traits of autism in the twins when they were aged 12. The twins completed four online language tests: the Figurative Language and Making Inferences tests taken from the Test of Language Competence (Wiig et al., 1989), which are designed to assess semantic and pragmatic language respectively, the Test of Adolescent Language (TOAL; Hammill et al., 1994), which is a test of adolescent language proficiency, and a vocabulary test derived from the Wechsler Intelligence Scales for Children (Kaplan et al., 1999). Multivariate twin model fitting explored genetic and environmental contributions to each measure individually, and estimated the degree to which traits of autism and language abilities share aetiological influences with one another.

Results: There was a modest phenotypic correlation between traits of autism and the four language measures ($r < 0.20$ in all cases [$p < 0.001$]). The best fitting multivariate twin model was a model that estimated the proportion of additive genetic, shared environmental (environmental influences that create similarities within a twin pair), and nonshared environmental (environmental influences that make two twins in a pair growing up in the same family different from one another) influences on each trait and which provided separate estimates for males and females. While traits of autism displayed high heritability, all four language measures displayed more modest heritability, and a considerable degree of nonshared environmental influences. Traits of autism showed low to modest overlap in genetic influence with all four language measures; all genetic correlations were in the region of 0.03-0.32. Shared environmental overlap was moderate, and nonshared environmental overlap was very low across all four language measures.

Conclusions: These results suggest that aetiological influences on traits of autism and language abilities are largely independent of one

another, meaning that it is likely that different genes and environments influence language abilities and traits of autism at age 12 years. These results have implications for molecular genetic endeavours, and may go some way to explaining the wide range of language skills evident in the ASD population.

127.090 90 Genetic Landscape of Autism: From a Novel Search Engine for Pubmed. J. Y. Jung*, T. F. DeLuca, T. Nelson and D. P. Wall, *Harvard Medical School*

Background: Genetics of autism involves hundreds of genes, and more than hundred Mendelian disorders are also associated with autism. While it is essential to review literature and to keep up with recently published ones in order to investigate this complex genetic landscape of autism, the number of publications related to autism has been drastically increased over the last decade and it hinders researchers from searching and reviewing them in a timely manner.

Objectives: We aim to build a publication search engine that specifically focuses on identifying target disorders and investigated human genes. In this case, we aim to identify all original research articles and reviews available in PubMed that examine links between autisms and genotype data, with minimal human intervention. The primary output of this pipeline is a list of autism candidate genes with significant results, supporting publications, and the main statements in such publications.

Methods: First, we built a disorder-specific query to use in PubMed with MeSH terms, expanded disorder aliases, and publication type filters in order to retrieve autism-related research articles. Next, we filtered genetics-related publications among them by matching genetics keywords, extracted from a training set of genetics-focused articles. We built and applied a rule-based text-mining algorithm to analyze titles, abstracts and MeSH terms in order to identify human gene symbols, negation/structures in the title and abstract text, and characteristics of the study (e.g., linkage analysis, gene expression, genome-wide association, copy number variations, etc.). Finally, we identified the main candidate gene(s) per each publication using structural information obtained in the previous step, and assessed the collective significance of each candidate gene

based on the number/importance of related publications and the type of study.

Results: Of 20,921 autism-related articles in PubMed, we identified 12,900 research-oriented publications and 5,155 articles of them turned out to be genetics-related, including 959 reviews. About half of them (2,542) included names or symbols mapped to human genes, and we found 784 research articles (excluding reviews) with 576 genes that report significant test result in either the title or result/conclusion section of the abstract. We compared our set of candidate genes and supporting publications with those of SFARI (manually curated) and HuGE Navigator Phenopedia (algorithm based). It turned out that our sets cover more number of publications including ones reporting negative associations, and we also found a number of significant candidate genes missing in both sites.

Conclusions: We implemented a PubMed search engine that can extensively search and summarize research articles, specifically focused on a given target disorder and human genome/genetics. This engine enables us to "see" the genetic networks of autism in terms of research publications, and works as a fundamental basis for conducting cross-disorder analysis between autism and other related complex disorders.

127.091 91 Inherited Rare Variants in Autism: Whole Exome Sequencing in Multiplex and Singleton Families. C. Toma*¹, B. Torrico¹, A. Hervas², A. Tristán¹, R. Valdés-Mas³, N. Balmaña², M. Maristany⁴, V. Padillo⁴, P. Romarís², X. S. Puente³, M. Bayés⁵ and B. Cormand¹, (1)*University of Barcelona*, (2)*Hospital Mutua de Terrassa*, (3)*University of Oviedo-IUOPA*, (4)*Hospital Sant Joan de Déu*, (5)*National Center for Genomic Analysis (CNAG)*

Background: Autism is a severe neurodevelopmental disorder which aetiology is mainly unknown. Twin and family studies suggest high heritability. To date a few autism risk genes have been identified, most of them found on the basis of overlap with other syndromic neurodevelopmental disorders, or because they are involved in chromosomal rearrangements or copy number variants (CNVs). Whole exome sequencing (WES) represents a powerful technology to identify rare single nucleotide variants (SNVs) that may help to depict the complex genetic architecture of autism. Recently, WES studies suggested novel autism candidate

genes through the analysis of rare *de novo* variants in singleton families. Although these studies represent pioneering insights into the genetics of autism, *de novo* variants do not explain the whole genetic complexity of the disease.

Objectives: In the present study we performed exome sequencing of 10 autism multiplex families with the aim to investigate the role of the inherited pool of rare SNVs and uncover new candidate genes.

Methods: The 10 multiplex families under study include 41 individuals, with 20 parents and 21 probands that fulfil diagnostic criteria for autism spectrum disorder (ASD). Structural variants analysis was performed in the affected individuals with the CytoScan HD array (Affymetrix) to exclude families with reported fully penetrant structural variants. To capture the exome fraction we used the NimbleGen SeqCap EZ Exome Library SR kit. The coding exons targeted corresponded to approximately 34 Mb. On average, individuals had 86% of target covered at >20X and 50% at >75X. Nonsense, frameshift and splice-site mutations were selected for Sanger validation, whereas missense mutations were previously filtered based on pathogenicity predictions. Our selection of inherited variants included only mutations present in both affected siblings. In addition, 20 singletons families have been studied in a second phase of this project.

Results: Our preliminary data indicate, as recently reported, that a cumulative effect of oligogenic heterozygous variants represents the most plausible genetic model for autism. In our study we found variants in genes already associated with syndromic autism such as *NF1* and *TSC1*, but also genes like *SCN1A* or *ANK2*, which have emerged recently as autism genes from exome sequencing studies. Interestingly, the data show that truncating variants may have a predominant role in psychiatric disorders. In fact, we found a correlation between a higher number of truncating SNVs and low Non-verbal IQ performance. Also, we found statistically significant differences between the number of truncating rare SNVs transmitted to both sibs and those that were not transmitted. Protein-protein interaction analysis of the identified SNVs pool, including truncating and

potentially damaging missense variants, suggested novel candidate genes for autism.

Conclusions: Our data suggests that truncating rare variants may have a major role in the aetiology of autism in multiplex families. This preliminary evidence is currently under study in an additional sample of 20 singleton families.

127.092 92 Maternal Genetic Effects On Autism Risk: Results From the Early Markers for Autism (EMA) Study. L. A. Weiss^{*1}, G. Desachy¹, K. Tsang¹ and L. A. Croen², (1)UCSF, (2)Kaiser Permanente Division of Research

Background: Studies of main genetic effects in autism have failed to explain the high heritability estimates for the disease suggested by classical twin studies and by correlation of broader autism phenotypes within families. Recently, researchers have begun to study the prenatal maternal environment as a risk factor in autism.

Objectives: We hypothesize that maternal genetic effects, including an interaction between maternal and offspring genetic variation (transgenerational epistasis), may influence susceptibility to autism. To test our hypothesis of maternal genetic effects in autism, we examined a sample of 400 mother-child pairs where the child has been diagnosed with autism and 400 matched control pairs where the child does not have autism.

Methods: Using the Affymetrix Axiom EUR array, we genotyped our samples at approximately 600k single nucleotide polymorphisms (SNPs) and performed copy number variant (CNV) calling. We performed two novel genome-wide association studies: first, we compared the mothers who had given birth to an autistic child to the control mothers (maternal genetic main effects) at SNPs and CNVs; second, we considered the maternal-child genotype combination at each SNP marker and performed several tests to see if the relative proportion of genotype combinations differed between case and control pairs (transgenerational epistasis). Specifically, at each locus we compared case and control cohorts using three models: 1) comparing the proportion of pairs that have identical genotypes, 2) comparing the proportion where the mother possesses an allele that her child does not possess, and 3) comparing the proportion where the child possesses an allele that the mother does not possess.

Results: No single SNP results were genome-wide significant ($P < 5 \times 10^{-8}$). For the test of maternal genetic main effects, we found variation within or nearby the following genes to be suggestive at the $P < 10^{-5}$ level: *MAML2*, *TMEM97*, and *XK*. For the tests of transgenerational epistasis, we found variation within or near the following genes to be suggestive at the $P < 10^{-5}$ level in at least one of our three models: *C4orf37*, *INSC*, *SLC7A8*, *GABRB3*, *GOT2*, *PALM2*, *KIAA0430*, *SLC14A2*, *SEMA3C*, *LY86*, and *CDH11*. In addition, we found variation in or near the following genes previously implicated in autism to be suggestive at the $P < 10^{-4}$ level in at least one of our three models: *MACROD2*, *NRXN1*, *RELN*, *GRIN2B*, *NLGN1* and *PCDH9*. In this sample, children with autism did not show significantly more CNVs than controls, however, we found that mothers of children with autism had significantly more deletions than control mothers ($P < 0.05$) and that this maternal CNV effect was replicated in data from family studies of autism, where mothers showed significantly more deletions than fathers in autism families ($P < 0.05$) in 2 of 3 datasets.

Conclusions: We have assessed a novel model for maternal genetic contribution to autism risk and found evidence for increased maternal CNV burden in autism families.

127.093 93 Glutamatergic Pathway and Axonal Guidance Signaling Genes As Candidate for ASD Etiology. C. M. Ribeiro*¹, A. L. B. Martins², V. N. Takahashi¹, D. P. Moreira¹, K. Griesi-Oliveira¹, C. Rosenberg¹, E. Vadasz³ and M. R. Passos-Bueno¹, (1)University Sao Paulo, Biosciences Institute, (2)UNESP, (3)Institute of Psychiatry, Hospital of the Faculty of Medicine, University of Sao Paulo

Background: The Autism Spectrum Disorders (ASD) are neuropsychological disorders, characterized by repetitive and stereotyped behavior, inability to communicate, lack of reciprocal social interaction and, sometimes, cognitive impairment. These disorders affect about 1/150 children, being currently considered a public health problem. It has recently been shown that *de novo* and mostly rare copy number variations (CNVs) accounts for about 10-15% of the autism cases.

Objectives: Identify new genes possibly candidate for ASD and verify what biological pathways can be significantly involved in these disorders.

Methods: It was analyzed 101 sporadic autism cases by custom-designed microarray CGH with a high probe density targeted to exon of genes previously reported as candidate for ASD and others involved in the same metabolic pathways of these genes. We included only patients with no history of complications during pregnancy, negative Fragile X result and without congenital malformations or facial dimorphisms. To assess whether detected alterations can be pathogenic, CNVs from ASD cases were compared to dataset from apparently healthy individuals (DGV) and 200 matched controls subjects analyzed by the same array platform. Only alterations not viewed in unaffected subjects were considered putative pathogenic and were validated using quantitative PCR, SNP array 500K from *Affymetrix* or CGH-array 180K from *Agilent Technologies*. The parents were also evaluated in order to verify the mutation origin.

Results: We detected 12 different CNVs possibly pathogenic in DNA samples from 17 autistic individuals. We observed enrichment of *de novo* deletions in genes whose proteins interact directly or indirectly with the neurotransmitter glutamate (4/12 - 33,3%). Among the functions performed by these proteins we emphasize: release of glutamate in the synaptic cleft, metabotropic glutamate receptor, catalyzing the production of gamma-aminobutyric acid from L-glutamic acid and glutamate transport into the pre-synaptic vesicle. Several other glutamatergic pathway genes have been reported as ASD candidates. We propose that dysregulation of these genes leads to an imbalance between excitatory and inhibitory synapses with consequent impairment of neuronal maturation and plasticity. We also observed enrichment of *de novo* deletions and duplications in genes involved in Axonal Guidance Signaling (3/12 - 25%). The roles performed by proteins of these genes are actin filament and cytoskeleton reorganization, dendritic spine morphogenesis and neurite outgrowth. Dysregulation of these genes can lead to synapse impairment.

Conclusions: Using the strategy of analyzing genes belonging to the same pathway of others already reported as associated to autism was possible to identify novel candidate genes. Furthermore, our results corroborate with the involvement of glutamatergic pathway and Axonal Guidance Signaling in the etiology of this disorder.

FAPESP/CNPq

127.094 94 Coalitional Games and the Relevance of Gene Expression in Autism Spectrum Disorder. F. J. Esteban*¹, L. Díaz-Beltrán² and D. P. Wall³, (1)*University of Jaen*, (2)*Universidad de Jaen*, (3)*Harvard Medical School*

Background: With the aim to provide a more powerful method for valuable signal detection in gene expression microarray experiments, a mathematical analysis of the gene expression data based into the coalitional (or co-operative) game area of game theory was recently proposed. The main advantage of this approach is the computed numerical index, called the Shapley value, which represents the relevance of each gene under a certain condition while simultaneous accounting for the expression behaviors of the other genes under the same condition, a method that, in combination with statistics, has been demonstrated to be useful for differential gene expression data analysis.

Objectives: To apply the coalitional game theory approach to determine the gene relevance on an ASD microarray experiment.

Methods: Using the coalitional game method previously described by others (Moretti et al. 2008; BMC Bioinf 9:361), we have analyzed a subset from experiment GSE6575 downloaded from Gene Expression Omnibus (GEO). This subset consisted of 17 samples of Autistic patients without regression and 12 healthy children from the general population. Statistical analysis was performed with Bioconductor (<http://www.bioconductor.org/>) in R (<http://www.r-project.org/>). We detected enrichment of biological function and overrepresentation of disease(s) among gene terms using Ingenuity Pathways Analysis (IPA; <http://www.ingenuity.com/>).

Results: Only two genes could be detected using standard statistical approaches. However, a relevant combination of 78 genes was obtained using the microarray game approach. IPA analysis identified 19 genes, in our set of 78 candidates, as significantly overrepresented in the general category of Neurological Disease.

Conclusions: Our results showed that coalitional games significantly increased the power to

identify candidates and that groups of these genes were associated with biological functions and disorders previously shown to be related to ASD.

127.096 96 Autism Spectrum Disorder in Duchenne Muscular Dystrophy. V. Ricotti*¹, M. Scoto¹, W. Mandy², K. Entwistle³, S. Robb⁴, E. Mercuri⁵, D. H. Skuse⁶ and F. Muntoni¹, (1)*The Dubowitz Neuromuscular Centre UCL, Institute of Child Health*, (2)*University College London*, (3)*UCL, Department of Clinical Psychology*, (4)*The Neuromuscular Unit, Great Ormond Street Hospital*, (5)*Child and Adolescent Neuropsychiatry Unit, Catholic University at Gemelli Hospital*, (6)*Institute of Child Health, UCL*

Background: Duchenne Muscular Dystrophy (DMD) is a recessive, X-linked muscle disease caused by a mutation in the dystrophin gene, which codes for the protein dystrophin. Dystrophin is an important structural component in muscle tissue, but is also expressed in the brain, and neurodevelopmental disturbance is common in people with DMD. Preliminary evidence suggests that autism spectrum disorder (ASD) may be highly prevalent in DMD, alongside difficulties with executive function and intellectual development. Furthermore, clinical observations suggest that the location of a person's mutation in the dystrophin gene may affect their risk of developing ASD and other neurodevelopmental problems. Specifically, we suggest that the further down the dystrophin gene the mutation, the more likely an individual is to have neurodevelopmental problems. Mutations downstream of exon 63 have the greatest impact on the production of forms of dystrophin that are expressed in the brain.

Objectives: To assess formally the prevalence of ASD in a sample of young people with DMD; and to test the hypothesis that mutations further downstream in the dystrophin gene carry the greatest risk of causing neurodevelopmental disturbance.

Methods: Participants were 112 (mean age = 9.5 years) boys with DMD, attending the neuromuscular outpatient departments at Great Ormond Street Hospital (London) and Gemelli Hospital (Rome). Parents completed the Social and Communication Disorders Checklist (SCDC) as a screen for ASD. Targeted neuropsychological assessments included: (1) Wechsler Intelligence Scale for Children-IV (WISC-IV); (2) the Dimensional, Diagnostic and Developmental

Interview (3Di); (3) the Conners-3; and (4) the Child Behaviour Checklist. Within this sample 39 had a mutation upstream of exon 30 of the dystrophin gene; 85 had a mutation between exons 31 and 62; and 12 had mutations downstream of exon 62.

Results: Forty per cent of the sample scored above the cut-off for probable ASD caseness on the SCDC screening measure. Subsequent detailed and rigorous assessment using the 3Di suggested a prevalence for ASD of 24% within this sample. Estimated rates of ADHD (35%) and internalising problems (30%) were also high. In addition general intellectual disability was found in 28% of the boys with DMD tested using the WISC-IV. SCDC score and intellectual ability were both associated with genotype: children who had a mutation downstream of exon 62 were most severely affected.

Conclusions: Rates of neurodevelopmental difficulties, including ASD, are elevated in DMD compared to general paediatric samples. Boys with mutations downstream of exon 62 have the highest risk of neurodevelopmental disorder, including autistic social communication impairment. Our findings highlight the need to clarify the role of dystrophin in neurodevelopment, and to investigate whether the gene-protein-brain-behaviour pathway we describe has relevance to cases of ASD outside of DMD.

127.097 97 Perturbed Cholesterol Metabolism in Autism Spectrum Disorders: Biochemical and Genetic Analyses. J. B. Rouillet^{*1}, A. Gunsul², J. Pearson³, T. Nguyen¹ and R. D. Steiner¹, (1)*Oregon Health & Science University*, (2)*OHSU*, (3)*University of Utah*

Background: Smith-Lemli-Opitz syndrome (SLOS) is a disease caused by mutations of the gene encoding 7-dehydrocholesterol reductase (*DHCR7*), resulting in accumulation of 7-dehydrocholesterol (7DHC) and impaired cholesterol synthesis. In an earlier study, we reported that as many as 85% of children with SLOS met criteria for an autism spectrum disorder (ASD). In a recently reported study, sterols were measured in a group of individuals with ASD, and although no sterol profiles were diagnostic of SLOS, low cholesterol levels (<5th percentile) were noted in approximately 20% of the study subjects. These studies suggest that cholesterol deficiency

or perturbed sterol metabolism is a risk factor for autism.

Objectives: The objective of the study was to determine if children with ASD have perturbed cholesterol metabolism or sequence variations in the *DHCR7* gene. We hypothesized that children with ASD would have lower plasma (pl-) cholesterol and 24S (24S hydroxycholesterol, a measure of brain cholesterol turnover) concentrations, elevated pl-7DHC, and a higher prevalence of the *DHCR7* sequence variants than children who came to the autism clinic for a evaluation for autism for which an ASD diagnosis was ruled out.

Methods: Case /control study consisting of 69 children (42 ASD, 27 non-ASD or controls) referred to the OHSU Autism Clinic for behavioral evaluation. Plasma cholesterol and 7DHC concentrations were measured by gas chromatography and 24-S-hydroxycholesterol (24S) concentration was measured by liquid chromatography-mass spectrometry. Sequence variants and pathogenic mutations of the *DHCR7* gene were identified by Sanger sequencing.

Results: The two groups were matched for gender, race and body-mass index (BMI). The median age was lower in the ASD group (30.7 months) than in controls (41.7 month, $p < 0.03$). Plasma cholesterol and 7DHC concentrations were similar in both groups, with low cholesterol levels (<5th percentile) noted in only 2.4% of the subjects with ASD (3.8% in non-ASD subjects). In contrast, 24S concentration was higher in subjects with ASD (104.1 ± 5.8 ng/mL) than in controls (78.6 ± 5.2 ng/mL; $p < 0.004$). This group difference remained statistically significant after adjustment for age ($p < 0.015$). Twenty-six participants (37.7% of the study population) were found to have either a single nucleotide variant or a mutation. The percentage of participants with either a mutation or a variant was significantly greater in ASD (21 subjects, 50%) than in controls (5 subjects, 19%, $p = 0.01$). Interestingly, only children with an ASD were found to have mutations. However, because there were only 3 mutations in the ASD group (7.1%), the difference with controls (no mutation) was not statistically significant.

Conclusions: The study does not confirm the previously reported high prevalence of low plasma cholesterol levels in ASD. However, brain cholesterol turnover may be higher in children with ASD, and *DHCR7* sequence variants are more prevalent in children with ASD than controls, suggesting that perturbations in cholesterol synthesis may predispose to ASD.

128 Innovative Technology Demonstration

128.098 98 A Meta-Analysis of Innovative Technology Based Interventions for Autism Spectrum Disorders. O. Grynspan*¹, P. L. Weiss² and E. Gal², (1)CNRS USR 3246, *Université Pierre et Marie Curie*, (2)University of Haifa

Background: The field of innovative technology based interventions for Autism Spectrum Disorders (ASD) is rapidly growing with the last decade showing a steep increase in the number of published studies. However, the field is still perceived to be “emerging”, and the clinical validity of many reported interventions has yet to be acknowledged by the wider ASD research and clinical community. This is due, in part, to the diversity of papers on this topic in terms of their goals and methods as well as to the interdisciplinary nature of the field that involves engineering design, developmental psychology and educational sciences.

Objectives: The goal of the present report was to carry out a systematic evaluation of innovative technology based interventions for ASD which would summarize the state-of-the-art and provide recommendations for improvements in methodologies for future research.

Methods: We used a meta-analytical methodology based on strategies that are recommended in clinical psychology. First, a systematic literature search was conducted via four major online databases with keywords including “computer”, “virtual reality” and “robotics”. The retrieved articles were selected for the meta-analysis if they involved evaluation of a computer-based technology intervention, included a group of participants diagnosed with ASD and assessed training based on a pre-post or randomized controlled trial (RCT) design. Case studies and studies relying on in-system assessments were excluded. In order to assess efficacy, we computed the effect sizes between post-tests of groups receiving the intervention and those of control groups who did not receive the

intervention. We also assessed the improvement following the intervention by calculating the within-group effect sizes between pre-tests and post-tests. We employed weighted effect sizes to account for sample size differences between studies. The homogeneity of the resulting effect size estimates was tested. The reliability of the results was evaluated by calculating the number of null studies needed to contradict the findings. We also conducted a moderator variable (age, IQ and duration of treatment) analysis to identify possible sources of heterogeneity between studies.

Results: The systematic search yielded 379 articles, out of which 21 were included in the meta-analysis. The test assessing efficacy in controlled studies was significant and yielded a mean effect size that approached the medium range (Cohen’s $d=0.47$, Confidence Interval= $0.08 - 0.86$). The mean effect size of improvements following treatment was also significant and approached the large range (Cohen’s $d=0.79$, Confidence Interval= $0.50 - 1.09$). The effect sizes of controlled studies were found to be heterogeneous. Although the influence of age and IQ moderator variables was not significant, the effects sizes correlated negatively with the duration of treatment.

Conclusions: The present meta-analysis provided evidence in support of the efficacy of innovative technology based interventions, especially for interventions related to desktop computer applications. However, research in the field needs to address the issues that account for the heterogeneity between studies. According to our analyses, sources of heterogeneity could involve treatment duration. This meta-analysis highlights the necessity that future studies adopt more standardized research designs and assess maintenance and generalization of acquired skills.

128.099 99 Detection of Animated Facial Expressions in a VR Game for Individuals with Autism. J. A. Crittendon*¹, E. Bekele², Z. Warren¹, A. Swanson³, Z. Zheng² and N. Sarkar², (1)Vanderbilt Kennedy Center, (2)Vanderbilt University, (3)Vanderbilt Kennedy Center; Treatment and Research Institute for Autism Spectrum Disorders (TRIAD)

Background:

Autism is characterized by atypical patterns of behaviors and impairment in social

communication. Prevalence is estimated at 1 in 88 for the lifelong disorder, which translates to tremendous costs to families and to society at large. Traditional behavioral intervention is intensive and limited in availability. Virtual reality (VR) has the potential to offer useful technology-enabled systems to help fill the gap between demand and supply. In VR, users can practice real-life scenarios in simulated settings that are carefully controlled. The importance of individualizing treatment remains one of the most robust findings for treatment success. VR technology can create a sophisticated, individualized user experience by monitoring user data and making dynamic adjustment in real time.

Objectives:

We designed a VR-based controllable program that collects performance, physiological, and eye gaze data as users complete social and daily living skills tasks. One objective is to teach users to make fast and accurate decisions about nonverbal communication during conversations. Understanding facial expressions (FEs) is a major component of nonverbal communication and is the focus of this investigation.

Methods:

Participants included children ages 13-17 who were in either an ASD (n=10) or control group (n=10). We created 7 avatars (4 boys, 3 girls) rigged with 7 facial expressions at 4 intensity levels (low, medium, high, extreme) for a total of 28 stimuli. Avatars first made a statement and then the animation was played. Statements were presented randomly with FEs such that users could rely only on the expression to classify the emotional expression rather than intonation or content of the statement. **Interactive demonstration of the program will be available during the presentation.** Data collected throughout the experiment included response accuracy, response time, eye gaze, and physiology (heart rate, GSR, pupil dilation, eye blink rate), and confidence ratings for each response.

Results:

The system successfully presented the tasks and collected the synchronized eye gaze and physiological data throughout. All participants, regardless of group, were best able to accurately identify sadness (90% accuracy both groups), followed by anger (ASD=75%, TD=70%), then disgust (ASD=73%, TD=63%), then joy (ASD=58%, TD=55%), and surprise (ASD=55%, TD=48%). Participants were least accurate on expressions of fear (ASD=43%, TD=23%) and contempt (ASD=18%, TD=15%). These data indicate children with autism named facial expressions with similar accuracy to controls. Further examination of the data, however, revealed participants in the ASD group had significantly longer response times and lower confidence ratings than did the TD control group. These group differences along with physiological and eye gaze data will be detailed.

Conclusions:

We developed a VR-based system wherein avatars were rigged with facial expressions at varying levels of intensity. The system was able to collect response accuracy, response time, physiological data and eye gaze patterns as participants completed the task. Data analyses revealed differences in the way children with ASD process and recognize emotional expressions compared to TD peers. Results will be used to inform refinement of the adaptive VR-based multimodal social interaction system. Implications of using VR as an adjunct to human-directed intervention will be discussed.

128.100 100 Representing Emotion in a Mathematics Tutor Designed for People with ASD by People with ASD. M. Brosnan^{*1}, E. Chapman¹, H. Johnson², B. Grawemeyer¹ and L. Benton¹,
(1)University of Bath, (2)U

Background: Recognizing and responding to the emotions of other humans has been argued to be a core deficit in Autism Spectrum Disorder (ASD), although evidence is mixed. For example, this deficit is not evident in simplified, distinctive animated representations of human-like emotion. Screen-based characters (digital personas) are often used within computer-based tutors to support learning. Representing emotionally-laden elements (e.g. a smiling face) within digital personas is typically motivating and beneficial to the user experience, resulting in enhanced learning. However, how emotion is best

represented within user interfaces and the impact of this emotion upon learning for people with ASD is not well understood. Firstly we involved adolescents with ASD in the design of the mathematics tutor, including a digital persona, using a process called 'Participatory Design'. This data accompanying the demonstration explored how representing emotion within a digital persona providing feedback within a mathematics tutor impacted upon adolescents with ASD.

Objectives: There were three objectives: Firstly to identify whether adolescents with ASD demonstrated a preference for feedback from a digital persona compared to text-based feedback; Secondly to identify if a digital persona enhanced learning compared to text-based feedback; and thirdly to explore whether the representation of emotion within the digital persona conferred any additional preference or learning benefits in adolescents with ASD.

Methods: This demonstration presents a technology that was used to assess user preferences and learning in twenty six adolescents with ASD under three conditions: 1) with a digital persona displaying emotion; 2) with a digital persona not displaying emotion; and 3) text only, with no digital persona present. All participants undertook all conditions, with the order of conditions counter-balanced across participants. Specifically, each condition involved users learning mathematics using a computer-based tutor designed by adolescents with ASD. The three conditions varied the nature of the delivery of feedback to users. Before and after each condition an evaluation of user preferences was conducted. The mathematics tutor also monitored performance in each condition, so that the number of correct responses to mathematic problems per condition could be identified. Finally, a paper-based pre and post mathematics assessment was conducted to evaluate if learning had generalized (over the three conditions combined).

Results: Adolescents with ASD preferred a digital persona and performed better (got more mathematics questions correct) when a digital persona was present, compared to when no digital persona was present. However, the two conditions with a digital persona present were the same.

Overall, learning did generalize to a paper and pencil assessment of mathematics.

Conclusions: Representations of emotion within the digital persona did not confer any additional benefits for adolescents with ASD. If the provision of emotionally-laden stimuli does not enhance performance, what aspects of the digital persona do facilitate performance (when compared to text-based feedback) in those with ASD? Overall the technology demonstrated did enhance learning of mathematics in adolescents with ASD that generalized to a pencil-and-paper based assessment.

Here we demonstrate the whole mathematics tutor system with the digital persona providing feedback upon mathematics performance.

128.101 101 Jestimule: A Serious Game with Innovative Human-Computer Interface Elements for Autism Spectrum Disorders. S. Serret*¹, S. Hun¹, G. Iakimova², J. Lozada³, M. Anastassova⁴ and F. Askenazy⁵, (1)Autism Resources Center PACA - Nice, (2)Anthropologic and Cognitive and social Psychology Department, (3)CEA LIST, (4)CEA List, (5)Child and adolescent psychiatry unit

Background: It is widely accepted that poor social cognition is a core problem in Autism Spectrum Disorders (ASD). An increasing number of studies have thus focused on the development of training programs and have shown promising results. Yet, most of these programs can only be followed by individuals with high-functioning ASD and/or Asperger syndrome, which correspond to 38% of the individuals in the spectrum. We have developed a social cognition training covering a large part of the ASD spectrum and thus challenging the obstacles of low intellectual and verbal ability. JeStiMulE is a multisensory computer-based game aimed at improving a wide range of social cognition abilities, including emotion, mental state and social context processing. It is based on innovative Human-Computer Interfaces (HCI). Both conceptual and technical innovations have been introduced to make the interaction natural, efficient, reliable and easy. A special focus was put on meeting the specific needs of people with ASD in terms of perception, communication and information processing. Thus, we introduced a color code to learn emotions and a device sending tactile messages with emotional value.

Objectives: The present study investigates the therapeutic application of JeStiMule to improve social cognition in a heterogeneous group of ASD. The usability of game platform is also tested.

Methods: 33 individuals with ASD, aged from 6 to 17, with an IQ from 40 to 129. They played with JeStiMule for 4 weeks (one hour twice a week). They were tested before and after training using social cognition tasks. These tasks included not only the game's avatars but also real characters, in order to investigate both the learning and generalisation potential of JeStiMule. The usability of platform game was evaluated by an HCI questionnaire.

Results: The results revealed a significant improvement on social cognition after using JeStiMule. This improvement could be observed for both avatars and real characters suggesting that the progress on social cognition has the potential to extend from the game to real-life settings. Importantly, this improvement was found to be IQ-, verbal- and age-independent. The results also revealed that the innovative HCI elements of JeStiMule were particularly adapted to the special needs of people with ASD.

Conclusions: JeStiMule can be beneficial to all individuals in the ASD spectrum, who are motivated to play.

128.102 102 ASC-Inclusion - Interactive Software to Help Children with ASC Understand and Express Emotions. S. Newman^{*1}, O. Golan², S. Baron-Cohen³, S. Bölte⁴, A. Baranger⁵, B. Schuller⁶, P. Robinson³, A. Camurri⁷, N. Meir¹, C. Rotman¹, S. Tal², S. Fridenson², H. O'Reilly³, D. Lundqvist⁴, S. Berggren⁴, N. Sullings⁵, E. Marchi⁶, A. Batliner⁶, I. Davies³ and S. Piana⁷, (1)*Compedia Ltd*, (2)*Bar-Ilan University*, (3)*University of Cambridge*, (4)*Karolinska Institutet*, (5)*Autism-Europe aisbl*, (6)*Technische Universität München*, (7)*University of Genova*

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, support a featured-based learning style of socio-emotional cues, and introduce cues separately in each perceptual channel. 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:

The ASC-Inclusion system is a virtual world that uses various educational and entertaining means to teach children with ASC to recognize 20 different emotions and express them through facial expressions, vocal intonation, body language and contextual information. The software is being developed by a consortium of leading organizations as part of a research project funded by the European Community's Seventh Framework Programme (FP7/2007- 2013).

Methods:

Training is performed through 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, using a standard microphone and webcam. 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.

The system's creation is supported by panels of families for children with ASC, and by panels of professionals, in Israel, Sweden and the UK, that contribute to an iterative process of development and evaluation.

Results:

The current presentation will demonstrate the system at its current stage of development, including its virtual world and emotion recognition training in the different modalities.

The environment, tutorials and games presented have been evaluated and approved by our panels of families and professionals.

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 will be carried out upon completion of the system's development.

128.103 103 Teaching Emotion Recognition From Facial Expressions Using a Realistic Robotic Head. A. Adams* and P. Robinson, *University of Cambridge*

Background:

Children with Autism Spectrum Conditions (ASCs) often have difficulty with face processing, including difficulty recognizing emotions from facial expressions. Some children with ASC also struggle to express their own emotions through facial expressions. Previous studies have attempted to address these issues by using a realistic robotic head in an intervention. However, these studies have only considered a handful of emotions while research suggests that there are hundreds of different affective states.

Furthermore, none of these studies has handed explicit control of the robot over to the child with ASC. Other research has shown that children with ASC tend to have impaired imitation abilities, and that interventions which incorporate imitation can lead to improvements in social-communicative behaviour.

Objectives:

To create an imitation system for children with ASC that provides three forms of facial expression interaction with the robot:

- (1) observing the robot acting out various emotions,
- (2) imitating the robot's facial expressions, and
- (3) controlling the robot's facial expressions through mimicry.

Facial expressions produced by the robot should cover a wide range of emotions and the ultimate goal of the interaction is to help teach emotion recognition to children with ASC.

Methods:

The imitation system takes video of a human face as input. In each video frame, it finds and tracks 66 feature points on the human's face in real-time. The system then translates the movement of those feature points into motor movements so that the robot's face mimics the video face in real-time. For the observation component of the interaction, the emotions and their corresponding facial expressions are animated on the robot using the short video clips from the Mindreading DVD developed by Golan et al. The DVD covers 412 different emotions and each emotion is acted out by six different actors. For the imitation and control components of the interaction, a webcam is pointed at the person seated in front of the robot and the live feed from the webcam is used to produce the robot's facial expressions.

Results:

Various techniques were investigated in order to achieve a realistic mapping from the movement of facial feature points in the video to the motor movements on the robot. The best technique (linear regression on a training set of non-rotated feature points) has been implemented in the final version of the imitation system. A controlled intervention study has yet to be run to determine the effectiveness of this imitation system in teaching emotion recognition to children with ASC.

Conclusions:

Our imitation system can perform facial expressions for 412 different emotions as well as real-time mimicry of facial expressions from a

webcam. The ASC-related experiments planned with the imitation system will allow the exploration of whether or not a robotic head is useful in teaching recognition of complex emotions, whether algorithms can help to coach expression imitation, and whether giving the child control over the robot has any effect on his/her engagement or anxiety levels.

128.104 104 NAO-Base: A Multimedia Database to Support Socially-Assistive Robotics for Individuals with Autism Spectrum Disorder. J. M. Vernon*¹, J. Kumar¹, C. R. Crowell¹, M. Villano¹, K. G. Wier², K. Tang¹, J. Zona³, D. C. Portenier³ and J. J. Diehl¹, (1)*University of Notre Dame*, (2)*Logan Center*, (3)*Barber National Institute*

Background: Socially-assistive robotics is a growing field that shows particular promise for use in therapy for children with autism spectrum disorder (ASD). Children with ASD: (a) show relative strengths in understanding the physical (object-related) world and relative weaknesses in understanding the social (interpersonal) world, and (b) seem to be more interested in treatment when it involves electronic or robotic components. At this point, social situations are so complex that the current state of robot technology and programming does not support the types of sophisticated social interaction necessary to have a robot act on its own in a seemingly autonomous fashion. However, if an interactive robot is controlled by a human, it is possible to have motivational benefits of the technology for children with ASD, while still targeting the disorder's characteristic social deficits.

Objectives: We will showcase a free, publicly available multimedia database that supports our therapeutically-relevant control system (DOMER, Villano et al., 2011) for a NAO robot (Aldebaran Robotics). For the past two years, the DOMER control system has been tested with 20 children with ASD. NAO-Base is a compendium of therapeutically-relevant robotic movements we have created for the NAO so that ASD researchers, therapists, schools, and centers can more rapidly implement our socially-assistive robot therapy system. All of the behaviors in NAO-Base can be utilized with DOMER.

Methods: We created DOMER, a graphical user interface that allows anyone to wirelessly control a NAO robot during an Applied Behavior Analysis (ABA) session. With DOMER, the interactive

responses of the robot allow for the simulation of real-time conversation between the child and the robot. We also created NAO-Base, which is a collection of all of the therapeutically-relevant robot behaviors developed during the course of our research. NAO-Base, which will be made available via a website, includes: (a) detailed description of each movement, (b) a file that contains the NAO movement commands needed to program the behavior, and (c) a video clip of the behavior so that users can see the movement being performed.

Results: NAO-Base is organized by categories of behavior. Currently there are five categories including Combination (61 behaviors), Non-Verbal (57 behaviors), Verbal (19 behaviors), Specialty Movements (24 behaviors), and Movements in Development (5 behaviors). Using DOMER to control the behaviors in NAO-Base allows the robot to respond quickly to social attempts made by the participant, with an average response time well under a second. Using this system and the NAO-Base behaviors, we have gathered clinical data, some of which has been presented at IMFAR previously (e.g., Tang et al., 2011; Klinepeter et al., 2012), indicating that many participants make notable gains in the social behaviors targeted for them during therapy. Moreover, we have been able to transfer this technology to two non-profit ASD programs that now use the technology.

Conclusions: Our free, publicly available NAO-Base greatly accelerates the process of utilizing DOMER to implement socially-assistive robot therapy because it provides access to a number of pre-programmed behaviors that have been tested in ABA therapy for children with ASD.

128.105 105 Exploring the Role of Computer Assisted Social Story Intervention On the Development of Social Communication Skills in Children with ASC. A. Constantin*¹, H. Pain¹ and A. Waller², (1)*University of Edinburgh*, (2)*University of Dundee*

Background: There is strong evidence that educational interventions can help children with ASC to acquire social communication skills and to become more independent. Social stories are widely used today, being a successful tool for developing and improving social communication skills in children with ASC.

Objectives: This research aims to explore how a computer-based application can support practitioners who work with children with ASC to build, present and assess social stories. The research questions addressed are as follows:

1. What are the practitioners' procedures and practices when working with social stories?
2. Can the technology facilitate the construction, presentation and assessment of social stories? If so, in which ways?
3. Does the computer-based technology enhance the practitioners' activity when using social stories?
4. Does the computer-based technology have a positive impact on the social communication skills of children with ASC?

Methods: A study with four teachers has been conducted, using task analysis and think aloud protocol, followed by semi-structured interviews. The empirical data have been analysed using Grounded Theory strategies (categorizing strategies, connecting strategies and memos). A combination of techniques (heuristic evaluation, cognitive walkthrough, query techniques and brainstorming) has been applied iteratively in various stages of the design to evaluate the low fidelity prototype and to improve it. An evolutionary prototyping approach is adopted to develop the system. Formative evaluation workshops with practitioners and children are taking place to continually refine the system. The final evaluation will be conducted in two steps. Firstly, an experiment will attempt to discover the effect of computer assisted social stories construction on teachers' activity. This will answer question 3. Secondly, a multiple baseline experimental design will be conducted with children with ASC. To answer question 4, the SCERTS assessment process (SAP) will be used to measure the impact of social stories on children's social communication skills.

Results: Preliminary results have revealed interesting ideas about how to facilitate and improve the construction, presentation and assessment of social stories using a software application. A computer-based application has

been built with two kinds of interfaces: one for teachers and one for children with ASC. Some of the main application features allow teachers to: create new social stories (with complete or partial sentences), choose to be guided through the construction of social stories or not, add customized rewards (using some libraries), annotate the sentences, assess and schedule social stories, add child's profile, or personalize existing social stories. Children can listen or read social stories either on computer or on paper. They can complete the partial sentences and get rewards.

Conclusions: Early data suggest that this computer-based application for social stories may have a positive impact on teachers' effectiveness (measured by the time required to accomplish various tasks, effort and resources). It is also anticipated that a computer assisted social story presentation will increase children's motivation and engagement resulting in the improvement of their social communication skills in a shorter time comparing with the same intervention using paper and pencil.

128.106 106 Storyscape a Social Illustrated Primer. M. Eckhardt*¹, M. S. Goodwin² and R. W. Picard³, (1)Massachusetts Institute of Technology, The Media Laboratory, (2)Northeastern University, (3)Massachusetts Institute of Technology

Background:

Communication impairments are a core challenge faced by individuals diagnosed with Autism Spectrum Disorder (ASD). These challenges result in difficulties in both the acquisition and expression of language. Within the ASD community, expressive communication ranges from complete mutism and little functional communication to highly skilled language expression. Furthermore, communication challenges extend beyond the person themselves and affect their family, friends, and larger social support network. While advances in communication technologies have transformed communication and connectivity for neurotypicals, the ASD community has had to hope for serendipitous advances in technology that can be appropriated. While cutting-edge learning technologies have moved towards technology-centered participatory cultures that facilitate learning at many levels, the ASD community has been largely left behind. This work presents a

technological ecosystem centered on a highly interactive and customizable story platform – StoryScape – that will allow a community of individuals to participate in the acquisition and expression of language through the exploration and creation of e-book stories.

Objectives:

The use of illustrated stories is a powerful and well tested method for teaching language and social situations for children diagnosed with ASD. The use of Social Stories and sequencing are common practice for many families, teachers, and therapists. StoryScape leverages these techniques and methods to create a new platform for creating highly interactive and personalized illustrated stories for use in learning language and social dynamics. Unlike current methods, StoryScape allows a community of users and content creators to participate in the teaching and acquisition of language. The objective of StoryScape is to leverage interactive personalized stories for the acquisition and expression of language.

Methods:

The development of StoryScape is following an iterative user-centered design methodology that include consultation with users, therapists, and education technology experts. Current work has been focused on initial development of an extensive platform that allows for story creation, story sharing, story remixing, and data collection and analysis. Planned experiments testing the efficacy of the system will proceed from initial design iterations and usability testing.

Results:

While experimental testing of StoryScape's efficacy in facilitating language acquisition and expression have not been concluded some initial test related to usability are under way. Preliminary results indicate that the platform is very intuitive to use for reading and interacting with the interactive stories. In addition, initial test have demonstrated that story creation is accessible to a wide area of people with different technological skill levels.

Conclusions:

The StoryScape project is a continuing work, initial development and usability testing are promising. The ability to easily create or modify learning material around a child's special interest is seen as a major advantage to engaging individuals in language centric activities. In addition, the platforms ability to record story interaction is very promising, as it allows for the collection of data that may reveal language and learning ability that otherwise would not be available. Further work is in progress to test the platforms ability to facilitate language acquisition and expression. During the poster session we will conduct live demonstrations.

128.107 107 Computer Supported Collaborative Conflict Negotiation Strategy Application for Adolescents with High Functioning Autism Spectrum Disorders. M. Hochhauser*, P. L. Weiss and E. Gal, *University of Haifa*

Background:

Adolescents with high functioning Autism Spectrum Disorders (HFASD) have difficulty in sharing affective experiences, negotiating and problem solving, all of which lead to problems in dealing with social conflict. This frequently escalates into social isolation and anxiety and difficulty in forming and maintaining meaningful relationships.

Objectives:

To examine the usability and sensitivity of CONTACT (Conflict Orientation Negotiation Training Among Children and Teens), a multi-user, collaborative application designed to identify, classify and treat conflict resolution skills within a technology-supported, constructivist learning environment. CONTACT is based on the COSPATIAL No-Problem authoring application (<http://cospatial.fbk.eu/>) with new content related to conflict resolution scenarios.

Methods:

During Phase 1, two focus groups, consisting of 6 healthcare professionals and 10 parents of adolescents with HFASD, were conducted to explore experiences related to conflict mismanagement which arise in this population.

The narrated vignettes were transformed into scripts which were then used to produce a series of videotaped scenarios that portray 12 scenes of typical adolescent conflicts during daily life activities, and three videotaped responses to each presented conflict. CONTACT is designed to provide the participants with opportunities to select, discuss and role play adaptive or non-adaptive strategies.

To date, 16 typically developed adolescents and 9 adolescents with HFASD, aged 12-18 years, completed two conflict questionnaires: CONFLICTALK and the Five Factor Negotiation Scale (FFNS, designed to measure adolescent conflict resolution styles. Thereafter the participants were presented with the 12 videotaped scenarios portraying social conflicts and asked to choose one of the following strategies for dealing with the conflict: a confrontational response, a submissive response, or a compromise-oriented response.

Subsequently they were asked to report on this experience by filling out the Intrinsic Motivation Inventory (IMI) task evaluation questionnaire that assesses a user's interest, enjoyment, perceived competence and satisfaction.

Results:

The results for the FFN conflict questionnaire showed that adolescents with HFASD were significantly less confident ($U = 35.5, P = 0.03$) than typical adolescents ($U = 35.5, P = 0.03$), demonstrated significantly fewer communication skills ($U = 27, P = 0.01$) and were less able to compromise ($U = 27, P = 0.01$) than typical adolescents when they reported how they resolved conflict. The results for the CONFLICTALK questionnaire showed that adolescents with HFASD showed significantly more passive and avoidance characteristics than typical adolescents when dealing with conflict ($U = 37.5, P = 0.04$). Similarly, in their responses to the CONTACT conflict scenarios, adolescents with HFASD used submissive strategies with significantly greater frequency than did typical adolescents ($U = 28, P = 0.01$). Finally, the IMI showed that the two groups had equivalent levels of Interest/ Enjoyment, Perceived Competence and Perceived Choice when using CONTACT but that adolescents with HFASD felt significantly greater pressure and

tension than did typical adolescents ($U = 20.5, P = 0.002$).

Conclusions:

CONTACT appears to be a feasible, user friendly and sensitive application for querying adolescents' responses to conflict.

128.109 109 Design of a Touch-Screen Computer Application to Develop Foundational Motor Communicative Skills. M. K. Belmonte*¹, M. Dhariwal², T. Saxena-Chandhok³ and P. Karanth³, (1)*The Groden Center*, (2)*National Institute of Design R&D Campus*, (3)*The Com DEALL Trust*

Background: Accessibility of computing technology comprises at least two components, economic and ergonomic. Until very recently these two aspects of accessibility have been at odds: cheap, mass-produced computers for the home market offered only a video monitor for visual-spatial output and a keyboard for motor-spatial or motor-symbolic input. Conventional keyboards demanded a high degree of fine motor skill and closed-loop proprioceptive-motor and/or visual-motor accuracy - a skill impaired in autism (Haswell et al., 2009). A monitor spatially distinct from the keyboard demands spatial re-mapping, and even touch-screen software usually assumes typical fine motor targeting and execution. A computer that can teach pointing amongst multiple response options in space, and sequencing these pointing actions to build symbolic representations, might provide a manual-motor communication alternative for persons with autism whose oral-motor dyspraxia may preclude communicative speech. **Objectives:** To design and pilot-test an iPad game that will develop the foundational skill of pointing to select amongst multiple response options, and the higher-level skill of representing objects with sequences of motor outputs, both in the manual motor domain of pointing and the oral motor domain of speaking, and in which movements of the client are distinguished from movements of the device by the therapist. **Methods:** The design exploits the autistic fascination with iconic rather than symbolic representations, and multi-sensory redundancies and sensory-motor contingencies, but avoids occasions for repetitive behaviour, and renders the communicative content spatially and temporally coincident with the most physically salient, attention-capturing stimulus (Chen et al., 2012). By pairing perception of the spatial

sequences inherent in jigsaw-puzzle pictures with production of the manual motor or oral-motor sequences making up the typed or spoken words for these pictures, the game aims to develop manual motor and oral motor skills and to bootstrap the development of symbolic from iconic representations. In several modes spatial sequences of jigsaw pieces can be dragged into place with a finger across the display, typed into place by pointing to sequences of characters spelling the object's name, or spoken into place by vocalising sequences of sounds in the object's spoken name. In all these input modalities, a high tolerance for manual targeting error or oral articulatory error is allowed. All manual and oral inputs from the user, as well as movements of the iPad itself, are logged. **Results:** The software is being piloted at two clinics specialising in autism spectrum conditions, in Bangalore, India and in Providence, Rhode Island, in clinically diagnosed autistic children ages 3 to 7 years who lack functional communicative speech. Initial measures, internal to the game software, suggest with continued game play decreases in motor targeting error and response latency and an increase in multiple-choice set size for successful responses. **Conclusions:** Mass-market touch-screen devices, combined with user interfaces that allow for open-loop, approximate motor performance, and with game designs that work with instead of against detail-oriented autistic cognitive profiles so as to develop skill at representing objects as symbolic sequences, can promote the development of communicative skills.

128.110 110 Dense Data Collection Through the Speechome Recorder Better Reveals Developmental Trajectories. I. Chin^{*1}, S. Vosoughi², M. S. Goodwin³, D. K. Roy² and L. Naigles¹, (1)University of Connecticut, (2)Massachusetts Institute of Technology, (3)Northeastern University

Background: Longitudinal designs are frequently used in developmental research; however, sampling at small intervals, or "microgenetic sampling," has often been underutilized. Less dense sampling rates distort developmental trajectories, as has been shown for infant's motor skills (Adolph et al., 2008). Sampling intervals thus affect the shape of developmental change; this is especially important in language research, where the type of trajectories that children undergo, such as the vocabulary growth spurt around 18 months, influences the theories proposed to explain

language development (Lieven and Behrens, 2012).

Objectives: The importance of microgenetic sampling was explored here through the use of the Speechome Recorder, which collects home-based dense, daily recordings of language use.

Methods: The Speechome recorded one child, Audrey between the age of 33-37 months. Audrey was diagnosed with ASD at 22 months but no longer met diagnosis at 32 months. A total of 34.14 hours of recorded interaction across 35 sessions ($M_{\text{length}} = 58.5$ minutes; $M_{\text{interval}} = 3.54$ days) was collected. Although installed in only one room, a variety of naturalistic child-adult interactions were obtained. Recordings were transcribed and coded for a number of grammatical features, including future tense.

Results: When examining data from all sessions, Audrey produced correct forms for the future, "going to" (60 instances) and "will" (66 instances), as well as an unusual frame "I'm a verb" (e.g. I'm a walk) 41 times. The developmental trajectories of all three forms were best fitted with a cubic model (adjusted R^2 between 0.94-0.98), but because the linear model also accounted for much of the variance (adjusted $R^2_{\text{will}} = .94$, adjusted $R^2_{\text{going to}} = .74$, adjusted $R^2_{\text{I'm a verb}} = .75$) subsequent analyses utilized the linear model. To investigate the effects of sampling rates on the shape of future tense development, data was selected at 7- and 14-day intervals (typical of language research; Lieven & Behrens, 2012). The longest session was chosen within that particular interval to provide the most data possible. With 7-day intervals, all three forms are shown to be growing in parallel, which is contrasted with the more variable trajectory revealed when all data are included (i.e., "Going to" and "will" alternate in growth until "will" supersedes "going to" at later sessions). With a 14-day interval, the growth curve was significantly different from the 'all data' one ($p < .01$). Therefore, the development of future tense looks drastically different when the sampling rate is increased.

Conclusions: The distortion of developmental trajectories by sampling rates was demonstrated

here by deviations from the original model when intervals were larger than 7-days, consistent with Adolph et al.(2008). Even when using the longest session, increasing sampling intervals altered the trajectory for each future tense form. Therefore, sampling rates can play a key role in the interpretability of research findings and smaller sampling intervals may be needed to accurately depict developmental trajectories. Tools that collect dense data such as the Speechome, allow for more accurate models and will play an important role in future language development research, especially in special populations where acquiring daily recordings may be difficult.

128.111 111 Analysis and Visualization of Longitudinal Physiological Data of Children with ASD. J. Hernandez*¹, A. Sano¹, M. Zisook², J. Deprey¹, M. S. Goodwin² and R. W. Picard¹, (1)*Massachusetts Institute of Technology*, (2)*Northeastern University*

Background:

Individuals diagnosed with Autism Spectrum Disorder (ASD) who have written about their experiences almost always describe immense stress and anxiety. Traditional methods of measuring these responses consist of monitoring the Autonomic Nervous System (ANS) of participants who behave compliantly in artificial laboratory settings. To the best of our knowledge, the study here is the first to conduct long-term monitoring and analysis of ANS in daily school activity settings with minimally-verbal individuals on the autism spectrum. ANS data obtained under natural circumstances can be very useful to provide warning indications of stress-related events and life-threatening events.

Objectives:

In this work we first test the feasibility of a longitudinal study in classroom environments using state-of-the-art biosensors to monitor ANS responses in minimally-verbal children with ASD. More specifically, we sought to explore the relationships between contextual events (i.e., different settings and activities), naturally occurring clinically relevant behaviors (e.g., aggression, self-injury, elopement), and physiological response patterns both within and between people over time.

Methods:

We conducted a two-month study (i.e., 60 continuous school days of recording for each child) with five minimally-verbal children (9-20 years old) at a non-profit school for individuals with ASD. In order to comfortably monitor ANS responses, we utilized the wireless Affectiva QTM biosensor, which simultaneously measures electrodermal activity (EDA), 3-axis accelerometer activity, and skin temperature levels. Beginning each school day, a sensor was placed on one of the ankles of each student and remained there until he or she departed. Teachers used a clipboard and a stopwatch (time synchronized with the Q sensors) to record settings (e.g., classroom, gym), activities (e.g., educational, physical activity), and clinically relevant behaviors (e.g., tantrums, aggression, elopement).

Results:

Over 60 days of recording, we obtained approximately 1,300 hours of physiological data and 6,000 annotations from teachers. In order to explore the large amount of data, we designed and developed a visualization tool that enables researchers to qualitatively analyze physiological data around different types of settings, activities, and before, during, and after observed behavioral episodes. Our presentation will demonstrate the Q sensor and our visualization tool, and provide preliminary findings within and between students relating to (1) heterogeneity in baseline arousal states over time; (2) relationships between autonomic changes and different observed behavior problems; and (3) associations between autonomic changes and cognitive demands of different activities.

Conclusions:

To the best of our knowledge, ours is the first attempt to gather long-term physiological data in a natural environment, in a population who usually has difficulty participating in laboratory studies, who frequently engages in challenging behaviors, and who struggle to provide any verbal self-report. To support the exploration of such a massive dataset, we engineered a new tool to enable more efficient data visualization. This visualization tool is used to help identify portions of the records that hold significance and that require further quantitative analysis. We will provide a sample of our initial analyses showing

both differences and clusters of similarity across individuals' ANS data over the two-month period.

128.112 112 Exploring the Interplay Between Autonomic Activity and Behaviors in Children with Autism Spectrum Disorder (ASD) Through a Multisensorial Platform for the Continuous Monitoring of Physiological Signals. L. Billeci*¹, G. Tartarisco¹, A. Narzisi², G. Baldus¹, D. Corda¹, F. Muratori² and G. Pioggia¹, (1)*Institute of Clinical Physiology, National Research Council (CNR)*, (2)*University of Pisa – Stella Maris Scientific Institute*

Background: There is a widely held assumption that ANS (Autonomic Nervous System) activity and behavioural manifestations in ASD subjects are closely related, but the relationship between the two is not yet well assessed and findings are contradictory. This study is part of the MICHELANGELO European Project, which is aimed to move the assessment and the therapeutic interventions from the clinic to a more "natural" home environment in which children are continuously monitored with unobtrusive technologies in order to establish a link between physiological and behavioural parameters for a personalization of the treatment.

Objectives: The main aim of this study is to explore connections between ANS and specific ASD symptoms, developing a collaboration between clinical assessment and engineering methodologies. In particular ANS activity is analysed acquiring unobtrusively, during social interactions, ECG and movement. A further aim is to characterize different phenotypes in ASD to suggest more tailored intervention strategies.

Methods: In this study we developed a naturalistic protocol based on imitation and joint attention tasks in which the child is free to move and interact with the therapist thanks to the unobtrusiveness of the acquisition system. Video, ECG and the movement of 8 school children (4 HFASD, rigorously diagnosed by an experienced clinic according to DSM-IV-TR and confirmed by the ADOS-G, and 4 typical controls) were simultaneously acquired during 20 min experimental sessions structured as: i) 5 min baseline (child still on a chair); ii) shared attention task; iii) imitation task (gestures and movements). Physiological data have been recorded with a wearable system implemented by the Institute of Clinical Physiology of the National Research Council of Italy (CNR) realized as a

chest strap placed at the level of the thorax embodying electrodes, electrical connections and a portable electronic board which acquires the signals and transmits data via Bluetooth to a PC for visualization, storage, analysis and transmission to a remote center. The system can visualize ECG and assess heart rate (HR), heart rate variability (HRV), the powers of high frequency (HF) and low frequency (LF), as well as the LF/HF ratio, allowing cardiac vagal and sympathetic activities as markers of autonomic interaction to be estimated.

Results: We observed that children, both typical and ASD, well accepted the system and the protocol and were able to perform the tasks without difficulties or constraints. Using the video we were able to link specific tasks and behaviours of each child with his/her physiological response. We observed a decrease of HR and an increase of HF during imitation tasks respect to the baseline in controls, while in ASD children there were not statistically significant differences.

Conclusions: The protocol applied in this study allows monitoring and correlating the behaviour and the physiological signals of the children in a naturalistic setting. The subtyping of ASD through an accurate description of these variables can help clinicians to identify which type of strategies work best for which subtype of ASD child and to adapt the environmental stimuli and the caregiver interaction to specific needs of the child.

128.113 113 Mindgamers in School. R. H. Rice*¹, L. I. Sugarman² and S. Jacobs², (1)*St. John Fisher College*, (2)*Rochester Institute of Technology*

Background:

Originally presented as a poster at IMFAR 2012, this project represents ongoing development of a therapeutic, physiologically-controlled video game that address autonomic and cognitive control issues in young people with high functioning autism (HFA). The game is intended to help young people with HFA learn skills to better manage anxiety and restrictive/repetitive behaviors (RRB). This project is supported by the Office of the Vice for Research and the Center for Applied Psychophysiology and Self-regulation at Rochester Institute of Technology.

MindGamers[™] integrates (1) a multi-sensor, FDA(US)-approved encoder for physiological inputs; (2) evidence-based principles for treating repetitive behavior and anxiety associated with HFA; (3) customizable avatars, assets and game worlds meeting the user's personalized therapeutic needs; and (4) a Dynamic Feedback Signal Set, (DyFSS); The DyFSS is a significant innovation that adjusts to each user's unique and changing "stress-profile." By integrating specific psychotherapeutic strategies with autonomic self-regulation, *MindGamers*[™] links learning adaptive behavior with stress-lowering skills. Player strengths are assessed and represented by tools chosen for a utility belt worn by a customizable Goal-Directed Inner Motivational Projection (GDIMP). Players also create a Problem-Based IMP (PBIMP) to represent a RRB in the game. This first game level takes place in a school setting.

Objectives:

The project's primary objective is to obtain feedback from young people 12-18 years of age with HFA on specific aspects of game design and play. These include: 1) which images are preferred to represent player strengths (i.e., on the utility belt); 2) which images are preferred to represent repetitive behavior (e.g., ears, eyes, body style, clothes, skin color of the PBIMP); and 3) preferences related to usability and biofeedback features.

Methods:

On three separate occasions between summer 2012 and spring 2013, subjects play the most current prototype of *MindGamers*. After playing the game, subjects complete a survey that asks for preferences related to objectives one, two, and three above. Data will be collected on customization preferences for the PBIMP, strengths, usability and biofeedback features.

Results:

Comparative analyses will be made by means of ANOVA for all continuous variables. Age, gender, and diagnosis will be used as control variables in an effort to reduce their impact on the results. If the sample size permits, exploratory factor analyses will be used to identify the dimensions of

variance represented in the data. Qualitatively, the feedback received from subjects will be used to refine game options, look, mechanics and feel.

Conclusions:

Individuals with HFA are attracted to interactive games and media. Research with video games suggests that young people with HFA are receptive to therapeutic strategies in these manageable and controlled virtual worlds. Importantly, evidence suggests that young people with ASD are able to translate lessons learned in virtual worlds to real world experiences. Most existing physiologically-controlled video games neither utilize physiological hardware licensed for clinical settings or precisely integrate evidence-based psychotherapeutic strategies. Furthermore, licensed biofeedback packages are generally not as engaging as available videogames. This project includes innovations that bridge these gaps with a physiologically controlled, customizable, therapeutic role-playing video game prototype.

128.114 114 Seeing the Doctor without Fear: Systematic Desensitization for Medical Visits in ASD. L. Boada*¹, M. Parellada², C. Moreno³, B. Villamia⁴, V. Pensosi⁴, C. Llorente⁵, J. Romo³ and C. Arango², (1)*Hospital General Universitario Gregorio Marañón. Instituto de Investigación Sanitaria Gregorio Marañón. IISGM. CIBERSAM*, (2)*Child and Adolescent Psychiatry Department, Hospital General Universitario Gregorio Marañón. Instituto de Investigación Sanitaria Gregorio Marañón. IISGM. CIBERSAM*, (3)*Hospital General Universitario Gregorio Marañón. Instituto de Investigación Sanitaria Gregorio Marañón. IISGM. CIBERSAM, Child and Adolescent Psychiatry Department, Spain*, (4)*Fundación Orange*, (5)*Child and Adolescent Psychiatry Department, CIBERSAM, Instituto de Investigación Sanitaria Gregorio Marañón, IISGM, Hospital General Universitario Gregorio Marañón*

Background: People with autism spectrum disorder (ASD) not only have greater medical needs than the rest of the population (Gurney, McPheethers and Davis, 2006), but they also have particular characteristics that make it very difficult for them to get the medical services they need (need for anticipation, lack of flexibility, problems identifying and describing symptoms, hypersensitivity to certain stimuli, stress over waiting times, etc.). Going to a medical visit can be a traumatic experience for people with ASD and their families.

Objectives:

1) To design, implement, and evaluate a program based on new technologies that make the medical environment more familiar and less stressful to the patients with ASD before, during, and after a hospital visit.

2) To evaluate the effectiveness of this program for reducing patient stress and anxiety, improving the family's quality care perception, and reducing medical visit time.

Methods:

I. Design "Doctor TEA" software built on a Web platform composed of a set of structured contents in film format of a real hospital, in 2D and 3D, showing the physical spaces, medical professionals, techniques, and instruments used for a medical examination, including many interactive games showing different aspects of a doctor's visit, such as a blood test.

II. Evaluation: Participants: 80 participants with autism spectrum disorder, Asperger's syndrome, or Pervasive Developmental Disorder-Not otherwise specified (PDD-NOS) (DSM-IV-TR and ADOS-G) recruited through the ASD Comprehensive Medical Care Program at Gregorio Marañón University Hospital in Madrid.

Procedure: Forty patients will use the "Doctor TEA" software for twenty sessions of 30-minutes over a 6-week period (experimental period). The other 40 will not receive any intervention. Participants in these two groups will be matched for clinical diagnosis, mental retardation, age, and type of medical specialist visit/test they will require. Following the experimental period, they will have their actual medical visit/test. Next, an evaluation will be performed in both groups using three specific questionnaires completed by families, patients (when possible), and a health professional. The main dependent variables will be: patient comfort perceived by the doctor/nurse, patient self-rated anxiety, next-of-kin rated anxiety, hyperactivity during the visit, time needed by the patient, etc.).

Results: At the present time, we are finishing the software development fully funded by Orange Foundation. By May 2013, the software development will be nearly complete and we will have preliminary results on the effectiveness of the software based on the dependent variables of the study.

Conclusions: Daily clinical practice demonstrates that with preparation and specific training in desensitization to medical procedures, patient anxiety is considerably reduced. The reasoning behind this program, which will be freely available to the public in the future, is to try to demonstrate that TIC can help people with autism to anticipate and understand medical visits and tests that any hospital or health centre may perform.

Note: Orange has already developed several software which are publicly available to facilitate the integration of persons with ASD (www.fundacionorange.es) and Hospital Gregorio Marañón has a specific program for the attendance of the medical needs of patients with ASD (Parellada et al, 2011; <http://ua.hggm.es/>).

128.115 115 Using Tic-TAC Software to Reduce Anxiety-Related Behaviour in Adults with Autism and Learning Difficulties During Waiting Periods. A Pilot Study. G. Herrera*¹, C. Campillo¹, C. Ramirez de Ganuza², J. L. Cuesta², R. Abellán¹, A. Campos¹, I. Navarro¹, J. Sevilla¹, F. A. Amati¹ and C. Pardo¹, (1)University of Valencia, (2)Autismo Burgos

Background:

The difficulties encountered by people with Autism Spectrum Disorders (ASD) in understanding the concept of time are well documented in the currently accepted descriptions of those disorders, in educational practice, and in personal accounts of people with ASD.

Objectives:

This pilot study evaluated the efficacy of the use of the software tool Tic-Tac (available from www.proyectoazahar.org), designed to make time visual, in three adults with autism and learning difficulties. This research focused on applying the tool in waiting situations where the participants exhibited anxiety-related behaviour.

Methods:

The intervention followed an AB design (baseline and intervention) and a partial interval recording procedure was used to code the presence of stereotypes, nervous utterances, wandering or other examples of nervousness during the selected waiting situations. Data were summarised in terms of the percentage of total intervals during which the anxiety-related behaviours were present. Inter-observer agreement was measured with the Pearson quotient at 0.81 between internal and external observers.

Results:

All three participants (William, John and Mary) demonstrated a reduction in their anxiety-related behaviours when Tic-Tac was introduced, although the level of improvement varied depending on the target behaviours. In the case of William there was a reduction from the 78.16% of intervals with stereotypical behaviours in the baseline to 32.21% when using Tic-Tac. In the case of John the percentage fell from 98.74% of intervals to a 67.36%. For participant 2, Mary, stereotypical behaviours were not so high at the baseline and no considerable reduction was found (from 40.20% to 37.27%). In terms of wandering and pacing, all three participants showed a reduction during intervention with Tic-Tac: William reduced his wandering intervals from 32.01% to 4.60%; Mary from 32.17% to 0.96%; and John from 83.14% to 16.67%. The average percentage of nervous utterances also fell for all participants: William demonstrated a decrease in this behaviour from 29.56% of intervals to 8.9%; Mary showed a slight reduction from 22.59% to 19.62%; and John from 44.53 to 21.25%. Finally, the other examples of nervousness also reduced during intervention with Tic-Tac, decreasing from 80.04% of intervals to 13.82% in William's case, from 48.86% to 23.65% for Mary and from 86.02% to 50.76% for John. No difference in the results was observed between longer and shorter waiting periods, meaning that the efficacy of the software was similar regardless of duration of use (from 3 to 10 minutes). In order to confirm that the anxiety-related behaviour was caused by the waiting situation and not by other factors, the Communication Notebooks and the Functional Analysis Record were reviewed in detail.

Conclusions:

The results showed that the use of Tic-Tac resulted in lower levels of anxiety-related behaviour in all 3 participants, compared to the baseline, suggesting that this software may be an effective technology for helping people with autism with organization and predictability during waiting periods. The present study demonstrates the positive impact of Tic-Tac with three participants with autism and justifies further work using bigger sample groups and different levels of abilities.

128.116 116 Mebook: A Novel Device Using Video Self-Modeling to Enhance Literacy Among Children with ASD. S. C. S. Cheung, J. Shen* and N. Uzuegbunam, *University of Kentucky*

Background: Reading books with children improves their literary skills. Children with ASD often cannot fully engage in the story due to off-task behavior and short attention span. Better self-regulation has been reported with interactive digital books or ebooks (Pykhtina et al., 2012). Ebooks open doors to the use of new sensors. This work focuses on an innovative use of a color-depth (RGB-D) camera to incorporate video self-modeling (VSM) into ebooks. VSM uses specially-prepared video of the child to model a target behavior (Dowrick, 1983). It is an evidence-based intervention shown to be effective for various learning tasks (Buggey, 2009). To combine VSM with ebooks, we propose to portray the reader as the protagonist of the story in a video shown next to the ebook. We hypothesize that the visual immersion of self into the story holds the attention of the reader and promotes self-regulatory activities.

Objectives: The aim is to build a video application, MEBOOK, to overlay features of the protagonist on the face of the reader and replace the scene background with animated video pertinent to the story.

Methods: MEBOOK runs on a computer equipped with a RGB-D camera. The depth data allows us to separate the reader from the background and track a 3D model of the face in real-time. We use the 3D model to insert synthetic objects that are geometrically aligned with the face independent of pose and motion. For example, the trunk of Dumbo can be visually attached to the reader's face. Also, the 3D model allows us to adjust the

viewpoint so as to create the illusion that the reader is looking directly at him or herself. The separation of foreground from the background is akin to the “green”-screen technology used in newscasts to substitute in a more suitable background, such as a real jungle video, while leaving the foreground objects intact. The user interface of MEBOOK has the rendered video next to the story text. Highlighted keywords allow the reader to change characters and background video.

Results: This study is to demonstrate the feasibility of MEBOOK, an application that utilizes a RGB-D camera to capture a 3D model of a child which is used to render self-video depicting the reader as part of a digital story. Using an appropriately chosen story, we will demonstrate the real-time response of the system, the overall quality and robustness of the rendering as well as the intuitive and engaging user interface of the overall application.

Conclusions: We have designed a software application, MEBOOK, to enhance digital story books with interactive visualization tools, making them suitable for children with ASD. The novelty is the use of the child’s face as a character in the story, a form of self-modeling, to engage the child in the story. A subsequent study to measure the effectiveness of MEBOOK in enhancing comprehension and self-regulation in reading among 5-7 years old children with ASD is underway.

128.117 117 Toby Playpad – Empowering Parents to Provide Early Therapy in the Home. S. Venkatesh^{*1}, D. Q. Phung¹, S. Greenhill², T. Duong¹ and B. Adams², (1)*Deakin University*, (2)*Curtin University*

Background:

Early intervention for children diagnosed with ASD is known to be critical. However waiting lists for therapy are long; the time between diagnosis and access to formal therapy can be as much as 18 months--a delay with immense societal cost. Parents are forced to endure this delay, feeling every lost day but lacking the knowledge and tools to redeem the time. We address the needs of families marooned in waiting lists by empowering the parent with knowledge and provide early therapy in the home.

Objectives:

We explore the design and implementation of the iPad application TOBY Playpad, a therapist-and-parent designed early intervention program administered at home by parents. It teaches a range of skills, both on and off the iPad, within a rigorous learning framework.

Methods:

A team of parents and research, technical and clinical therapists collaborated over two years to design and iterate TOBY Playpad. In that time, three trials, each granting a greater degree of autonomy to the participants, have been used to evolve its design and verify its impact:

The core features of the implementation are:

- A rigorous learning framework for defining, delivering, and recording: stimuli, responses, prompting and reinforcement.
- A multi-skill syllabus covering visual and auditory understanding, receptive and expressive language, imitation and social skills, totalling 52 skills taught in 320 tasks, completely specified in the form of a fine-grained dependency tree.
- Algorithms for delivering the syllabus flexibly in response to each child's performance, including: Prompting levels that adapt relative to performance; Reinforcement that adapts relative to performance, at individual trial and task levels; and Measurable criteria for mastery and progression through the syllabus.
- Natural Environment Training co-ordinated with on-iPad tasks to teach skills in the real-world, helping children to retain and generalize skills.

TOBY Playpad aims to empower parents to assume the role of therapist by: supplying *knowledge* in the form of a comprehensive multimedia help resource; a mixed-initiative therapy *planning* model that gives direction while allowing for the contingencies and varying circumstances of daily life; providing rich *progress reports* to help guide planning choices; and

programmatic support of the core aspects of ABA & DTT encoded in, e.g., mastery criteria, progression logic, and session recording; and a token-reward system that reinforces learning.

Results:

Three formal trials (n=8, 16, & 47; ages 2--8) have led to the following outcomes:

1. The instructional design and learning framework enabled a majority of children to learn skills over time.
2. Learning was tracked accurately, areas of difficulty were identified, and stimulus delivery was accordingly concentrated on those areas, while allowing children to move at their own pace.
3. Natural Environment Training complemented iPad-based tasks and integrated with daily life.
4. Parents expressed the sense of empowerment TOBY afforded them.

Conclusions:

This work delivers technology that helps parents administer a therapist-designed program at home. Through principled delivery, it is able to cover a large range of core but complex early learning skills. Critically, it fills the gap when crucial intervention time would otherwise be wasted.

128.118 118 Interest of Kinect in Psychomotor Development of Children with ASD. T. Maffre*, J. Perrin, L. Franchitto and J. P. Raynaud, *CHU de Toulouse*

Background: Children with ASD have a disorder of psychomotor development that commands the implementation of a specific rehabilitation. However, the children with severe intensity ASD and intellectual disability show usually significant difficulties of participation that can limit the impact of these rehabilitations.

Objectives: The objective of this exploratory study is to evaluate the benefit of using the kinect in a psychomotor rehabilitation towards these children. More specifically, it is to determine whether, on one hand, the kinect is a motivating learning for these children, and on the other hand, whether

psychomotor learning can be acquired with this technology.

Finally, a secondary objective is to assess whether:

- The mere repetition of the use of the Kinect without rehabilitative intervention allows to improve performance in games used.
- Improving the games scores can result in changes on the psychometric level

Methods: 4 children with severe intensity ASD associated with moderate to severe intellectual disability participate in this study. These children have roughly equivalent developmental levels. Psychomotor skills were initially assessed using standardized tests in the areas of motor skills, executive functions and imitation. A retest composed of the same instruments will be made at the end of the program

A kinect game has been proposed for 15 minutes during 12 sessions of psychomotor rehabilitation. This game implements the following skills:

- Anticipation
- Motor Coordination
- spatial recognition.

These areas of expertise were not trained specifically during rehabilitation sessions except when using the Kinect. An observation checklist was developed to assess the development of these skills in the protocol, as well as the level of motivation on the basis of a checklist of observable behaviors.

To provide a baseline, the kinect game has been first offered to children without guidance. Systematic quotation of the observation frame made it possible to assess their ability to learn independently.

A phase of play with psychomotor guide was then introduced at meetings No. 3, No. 4, No. 5 or No. 6 according to the children. Systematic quotation of the observation scale was used to assess the evolution of skills under the guidance and the effect of therapist.

At the end of the protocol, a re-test of psychomotor skills has been proposed to determine whether the development of skills sought by the game resulted in an improvement of psychomotor skills

Results: We aim to check several assumptions:
-Children with severe intensity ASD are motivated to psychomotor learning through the use of kinect
-The guidance and support of the therapist are

needed to improve their success in the game and improve updated skills

- Improved game scores reflects the development of psychomotor skills which can be demonstrated by the retest of targeted abilities

Conclusions: Regular use of the KINECT is likely to improve psychomotor skills of children with ASD if it is mediated by a therapist

128.119 119 Loris: Web-Based Neuroimaging Data Management for Autism Research. P. Kostopoulos*, C. Rogers, S. Das and A. C. Evans, *Montreal Neurological Institute, McGill University*

Background:

LORIS is a web-based data management system that has been used internationally as the backbone for a number of large-scale neurodevelopmental studies including the NIH MRI study of normal brain development (Das 2012; Evans 2006). Currently, LORIS provides a framework that houses data for more than 10,000 unique subject profiles, with data collected on over 500 behavioral and clinical measures.

Objectives:

Specific features of the database have been customized and further developed in recent years for autism research and deployed in the Infant Brain Imaging Study (IBIS)³ that studies brain behaviour correlates in infants at high risk for autism, and the Autism Spectrum Disorder project for NeuroDevNet that investigates the brain and behavioural development in affected individuals (Wolff 2012). In these longitudinal studies involving data collection across multiple sites, it is critical to provide rigorous and extensive data management systems that facilitate quality checking and validation of collected data. To this end, LORIS incorporates modules that ensure data quality and facilitate the uniformity of data within each project.

Methods:

For both behavioral and neuroimaging modalities, quality control and extensive validation mechanisms provide detailed, timely and informative feedback at the level of each entered variable, and improve data collection going forward.

Results:

First, at the data entry level, restricted data options, strict input controls, and range checking enforce data consistency according to project standards. Automated scoring and normative look-up tables ensure proper scoring, double data entry reduces errors, and strict completion rules ensure the completeness of the data. All of these features guarantee the quality of stored data and reduce the need to revisit data with corrective action.

Once data is entered, separate modules have been designed for data validation and feedback based on automated and manual checks. Through a web-accessible user-friendly module, researchers can quickly review data completeness, integrity, and validity, and flag cases that need further examination. In addition, the statistics module provides a quick overview of the data, while user-defined scatterplots can be displayed for visual verification of the data.

Finally, a separate module has been designed to ensure that the clinical data acquired are validated against a "gold" standard of reliability, as well as for within-project reliability. This reliability module helps with verification and administration of reliability on important clinical measures such as the Autism Observational Scale for Infants (AOSI), the Autism Diagnostic Observation Schedule (ADOS) and others. Through a web-accessible video and document repository, clinicians can download cases to review and provide validation responses directly in database. Enforced by project-defined regulations and thresholds, the reliability module enables monitoring, recording and reporting of within and across site reliability, ensuring that clinical data is valid and reliable across the project.

Conclusions:

In summary, a series of database features within the LORIS data management system have been customized for the use of multisite, longitudinal projects in autism and have demonstrated great benefit. Given the direction of autism research towards multimodal research that takes advantage of newly established networks, such infrastructure is critical to ensure quality of data and facilitate collaborations.

128.120 120 Integrated Data Management Processes for Autism Research: Empowering Efficient Data Reuse and Sharing Across Multiple Studies, Data Types and Sites. J. Hawthorne*, D. Voccola, N. Sinanis, F. Farach and L. Rozenblit, *Prometheus Research, LLC*

Background: A typical data management challenge for the past 25 years has been organizing data from a single study with a single data type for analysis. Upon completion, the data was archived with no expectation of reuse. Just-in-time (JIT) data management practices, such as cleaning and organizing data immediately prior to use, were adequate. Today, however, the demand of translational research in autism requires investigators to (1) integrate multiple data types from multiple sites and/or studies and (2) reuse and share their data. When applied to modern translational autism research, JIT processes are inefficient and compromise data quality. We sought to optimize these activities through a set of procedural changes, made possible by an integrated data management system (iDMS).

Objectives: Our goals were to (1) make high quality data sets accessible within minutes rather than weeks or months; (2) reduce redundant data manipulations for simple revisions to a research question; and (3) implement a transparent and reproducible mechanism for data regeneration.

Methods: We developed an iDMS that can accommodate multiple studies, heterogeneous data types, and multi-site collaboration. We implemented processes that encouraged up-front data cleaning at the time of acquisition, including data integrity constraints, improved electronic data capture, and data quality reporting. The iDMS and processes have been adopted by several research groups; we reviewed the use of the iDMS by two data managers to fulfill a range of requests for clean data sets by investigators. The data managers produced multiple data sets over the past year, and the average time it took to complete each was recorded. The recorded time included investigator communications and query revisions.

Results: Our solution was to (1) centralize all data sources into a single database; (2) clean the data once, up-front; and (3) enable data managers to easily construct and save complex queries. These three procedural changes reduced

the time required to produce a data set. Though quantitative measures are unavailable for the "before" state, anecdotal evidence strongly suggests that producing each data set using the JIT process took weeks or months. With an iDMS, the average time per request was 5.8 hours for the 85 ad hoc data set requests. Interestingly, 33% of requests took 30 minutes or less to complete. Additionally, data quality was higher as a consequence of upfront cleaning and staff allocation was lower due to elimination of redundant data cleaning activities. The queries could be saved in the system and later reused for revisions and comparisons.

Conclusions: Adopting an integrated data management (iDM) process with a compatible system can significantly reduce costs and increase data quality. The greatest challenge was integrating data sources with varying degrees of cleanliness. Data cleaning and organization are likely to remain challenging, as the number of data sources to manage continues to increase. We expect iDM practices will be most valuable when both the cost of data acquisition and the probability of reuse are high. We believe the efficiency gains described here will accelerate scientific discovery and translation.

128.121 121 Architecting an Open-Source Research Exchange Database (RexDB): How to Design a System That Supports Integrated Data Management for Multidisciplinary Autism Research. L. Rozenblit, F. Farach, D. Voccola* and C. Tirrell, *Prometheus Research, LLC*

Background: The need for effective, centralized management of biomedical and behavioral research data has expanded dramatically in the past decade, especially in interdisciplinary areas like autism research, where longitudinal and multi-center projects require secure, flexible data management and sharing platforms. However, current solutions are either too expensive or insufficiently flexible. Our team has developed an integrated data management platform that has been used at over a dozen leading autism research centers over the last 7 years. In late 2011, we began to package this platform as an open-source project to make it freely available to all autism research centers and programs. Defining a suitable high-level architecture for this platform was a key early challenge.

Objectives: Design a high-level architecture for the open-source RexDB platform that will: (1) communicate key functionality to stakeholders; (2) define clear boundaries and interfaces between components; (3) support all the key functions of integrated data management including data acquisition, integration, curation, and use; (4) support configuration of studies and instruments by non-programmers; (5) support extensibility by third-party developers; and (6) encourage adoption of the open-source platform by the research/data manager/developer communities.

Methods: We reviewed publicly available architectures for several relevant projects and extracted key insights. We then created several mock architecture diagrams and reviewed each for technical feasibility, communication effectiveness, and compliance with the architectural objectives. After an internal review, we conducted a focus group to gather input from relevant stakeholders.

Results: Internal and external feedback suggested revisions to the architecture that were implemented as a consensus solution. The resulting architecture separated out the data acquisition component as a stand-alone system, RexAcquire. This system has minimal dependencies, does not require a database, and can be scaled quickly across many servers to support very large simultaneous data collection efforts. RexAcquire consumes configuration files that specify the instruments to be administered and their display logic; it emits raw measure results files. The largest component, RexCollect, encompasses the major data integration and curation functions, including instrument and study configuration, data transform rules, data quality checks, and user management. It consumes the raw measure data files emitted by RexAcquire and transforms them into appropriate relational data structures; it emits instrument configuration files that RexAcquire consumes. RexCollect also allows users to select large subsets of data across studies, data types, and sites, and generate new temporary relational databases for exploring the extracted subsets. Another relatively stand-alone component, RexPlore, supports the exploration of the extracted subsets and generation of tabular data sets for statistical analysis.

Conclusions: A platform architecture must attempt to balance many competing forces. Functionality, technical feasibility, and communication effectiveness rarely pull a design in the same direction. We developed and applied a process that attempts to balance these competing demands in an open-source project by involving various stakeholders early in the design process. The result is an architecture that we believe is a better compromise, and that will contribute to the success of RexDB as a common integrated data management platform for autism research.

128.122 122 Rex Acquire: A Configurable, Open-Source Data Acquisition Platform for Integrated Autism Data Management Environments. D. Voccola*, C. Tirrell, O. Golovko, C. Evans, O. McGettrick and L. Rozenblit, *Prometheus Research, LLC*

Background: The collaborative, multidisciplinary, and often longitudinal nature of autism research requires a data acquisition platform that is secure, scalable, extensible, and reusable across multiple studies and domains. We evaluated existing systems (such as REDCap, ISAAC, and AdvantageEDC) and found that none fit the needs of complex interdisciplinary or translational projects. No existing platform offered the combination of features that included interactive, user-driven configuration; open-source licensing; and thoughtful support for integrated data management across studies, data types, and sites. To address this deficit we packaged and open-sourced the Research Exchange and Acquisition Platform (RexAcquire), a secure Electronic Data Capture (EDC) system with integrated data management features.

Objectives: We aimed to (1) deploy and host a HIPAA-compliant EDC platform on the Web that is reusable across multiple research studies; (2) configure the platform to store results from standard and experimental research instruments and questionnaires; (3) configure the platform to present EDC forms to both research participants (single-entry) and research staff (dual-entry), with screens optimized for each audience; and (4) automatically push research data into an Integrated Data Management System (iDMS), such as RexDB®.

Methods: To achieve our aims we (1) engaged with autism researchers through structured and unstructured interviews and focus groups to

define requirements; (2) packaged the software platform as an open-source project by re-architecting the code, documenting it heavily, and releasing it on BitBucket, a public code repository; (3) evaluated the platform at test sites by collecting user feedback and reviewing support histories; and (4) facilitated the creation of an active user/developer community around the open-source platform by promoting the platform at conferences and online channels.

Results: We have completed steps 1 and 2. Step 2 was accelerated by the ability to build on top of an existing code-base: the Prometheus Reusable Online Assessment Delivery System (ROADS), which has been used on a variety of major projects, including the Simons Simplex Collection. However, building an open-source project starting with existing proprietary code posed some unique challenges to architecture and documentation. We have also made significant progress on steps 3 and 4. Preliminary findings show test sites are able to use RexAcquire as intended. Users have configured over a dozen instruments and report that the system is “very user friendly” suggesting good usability. The software is freely available for download, use, and modification as part of the open-source RexDB package at rexdb.org.

Conclusions: The early results of the open-source RexAcquire project are encouraging, and indicate that RexAcquire supports all of the stated objectives, including interactive user configurability, the efficient reuse of research instruments from multiple studies and data types, and the transfer of data into an integrated data management system (RexDB). Anecdotal evidence strongly suggests that RexAcquire can serve to bootstrap an organization’s transition to an integrated data management approach. Immediate next steps include evaluating objective indicators of activity in the open-source community and continued field testing.

Brain Imaging Program

129 Brain Imaging - Structure/Function Correlation

129.123 Altered Functional and Structural Brain Network

Organization in Autism. J. D. Rudie^{*1}, J. A. Brown¹, D.

Beck-Pancer¹, L. M. Hernandez¹, E. L. Dennis¹, P. M.

Thompson², S. Y. Bookheimer¹ and M. Dapretto¹,

(1)University of California, Los Angeles, (2)UCLA School of Medicine

Background: Structural and functional underconnectivity have been reported for multiple brain regions, functional systems, and white matter tracts in individuals with autism spectrum disorders (ASD). Although recent developments in complex network analysis have established that the brain is a modular network exhibiting small-world properties, little work has been done to characterize network level properties of functional and structural brain organization in ASD.

Objectives: Here we investigated functional and structural brain network organization in children and adolescents with ASD compared to matched typically-developing (TD) controls.

Methods: We used resting-state functional MRI (N=42 ASD, N=37 TD) and diffusion tensor MRI derived fiber tracts (N=51 ASD, N=43 TD) in a 264-region whole-brain parcellation to examine pairwise differences in functional and structural connectivity as well as differences in higher-level network properties using graph theoretical methods. Additionally, we examined the correspondence between structural and functional connectivity and the relationship between network properties and chronological age.

Results: Children and adolescents with ASD displayed reduced short and long-range connectivity *within* functional systems (i.e., reduced functional integration) and stronger connectivity *between* functional systems (i.e., reduced functional segregation), particularly in default mode network and higher-order visual regions. Pairwise group differences in functional connectivity are reflected in network level reductions in modularity and clustering (local efficiency), but shorter characteristic path lengths (higher global efficiency). Structural networks displayed lower levels of white matter integrity yet higher numbers of fibers in children with ASD. TD and ASD individuals exhibited similar levels of correlation between raw measures of structural and functional connectivity (N=35 ASD, N=35 TD). However, a principal component analysis combining structural and functional network properties revealed that the balance of local and global efficiency between structural and functional networks was reduced in ASD, positively correlated with age, and inversely correlated with ASD symptom severity.

Conclusions: Our findings suggest that complex network modeling of structural and functional brain organization will yield a better understanding of the neural basis of ASD and other neuropsychiatric disorders. Ultimately, a more cohesive framework for understanding brain alterations in ASD may inform the design of more sophisticated diagnostic tools and targeted interventions.

Rudie J.D., Brown J.A., Beck-Pancer D., Hernandez L.M., Dennis E.L., Thompson P.M., Bookheimer S.Y., Dapretto M., (In Revision). Altered Functional and Structural Brain Network Organization in Autism. *Neuroimage Clinical*.

129.124 124 Corpus Callosum Structure and Interhemispheric Information Transfer in Autism. E. B. Barbeau^{*1}, J. D. Lewis², A. C. Evans², L. Mottron¹ and T. A. Zeffiro³, (1)*Centre d'excellence en Troubles envahissants du développement de l'Université de Montréal (CETEDUM)*, (2)*McGill University*, (3)*Neural Systems Group, Massachusetts General Hospital*

Background: Although behavioral evidence supports the notion that interhemispheric information transfer is atypical in autism, the neural mechanisms responsible for these phenomena are unclear. One of the most common neurostructural findings in autism involves the corpus callosum (CC), the main white matter fiber bundle connecting the hemispheres. In autism both CC size and fiber integrity are atypical, suggesting that information transfer efficiency may be adversely affected. However, direct evidence supporting a link between atypical structure and interhemispheric information transfer is lacking.

Objectives: To investigate the relation between task performance requiring interhemispheric information transfer and the length, size, and integrity of the callosal fibers in autism.

Methods: 22 autistics and 23 non-autistics were studied, with the groups matched on Wechsler PIQ (77-127), Raven's Progressive Matrices, age (14-38) and laterality. Visuomotor tasks requiring interhemispheric information transfer included: (1) the Purdue Pegboard Test, involving hand-eye coordination and bimanual coordination, and (2) the Poffenberger Task, measuring interhemispheric transfer time, based on the principle that reaction time to a stimulus

presented in the visual periphery is faster when the involved visual and motor cortical areas are in the same hemisphere than in opposite hemispheres (where interhemispheric information transfer is required). White matter microstructure was studied with diffusion tensor imaging ($b=0$ and 700s/mm^2 , 128 directions) and callosal macrostructure with high-resolution T1-weighted images collected using a 3T MRI system. The size of 25 CC subregions was determined from the T1-weighted images, and their microstructural integrity was estimated from the diffusion images. The surface area of the cortex to which each CC subregion projected, and the corresponding fiber length, was computed using probabilistic tractography. The size of each CC subregion (relative to the surface area of the left and right gray matter regions it connects) and its diffusion properties were then related to the behavioural measures of interhemispheric transfer using linear models.

Results: Relative CC size was significantly smaller in autistics compared to controls in frontal subregions connecting the motor cortical areas. For fiber length, no group differences were observed. As expected, in controls, bimanual task performance (Purdue) was positively correlated with the size of the CC in the subregions connecting sensorimotor cortices. However, for autistics a negative relationship between motor performance and CC size was observed in regions connecting occipital cortical areas. Although interhemispheric transfer time (Poffenberger Task) was related to CC size in sensorimotor regions for controls, it was more strongly related to the length of the CC fibers connecting occipital areas in autism.

Conclusions: Different relationships between regional CC macrostructural properties and visuomotor behavior in autism suggest that associated CC size reductions reflect atypical interhemispheric connectivity. Stronger visuomotor behavioral correlations with CC regions connecting visual areas in autism supports the existence of an atypical pattern of interhemispheric information transfer, possibly reflecting a more prominent role for visual mechanisms in sensorimotor behavior.

129.125 125 Individual Differences in Anxiety Symptoms Predict Amygdala Function in ASD. J. D. Herrington^{*1}, A. N.

Browne¹, C. M. DeLussey², V. Troiani³, G. K. Bartley¹ and R. T. Schultz¹, (1)*Children's Hospital of Philadelphia*, (2)*The Children's Hospital of Philadelphia*, (3)*University of Pennsylvania*

Background: Although many of the biological systems supporting social functions also support basic emotion processes, there have been few attempts to date to understand the "social brain" in ASD in terms of these processes. The absence of data on emotion systems in ASD is highly problematic, as anxiety disorders are common in ASD, but lead to a distinct set of predictions on amygdala and medial prefrontal cortex function that do not fit squarely within social brain models of ASD. Individual differences in anxiety symptoms may prove critical to our understanding of how deficits in social brain structures contribute to the clinical presentation of ASD.

Objectives: The present data test for a relationship between anxiety symptoms and social brain function (namely amygdala) among individuals with ASD.

Methods: Data from multiple functional MRI studies of ASD with and without co-occurring anxiety symptoms are presented. Although data collection is ongoing, the present sample includes 42 children with ASD ranging in age from 7 to 17 years (mean age = 12.3 years). fMRI tasks use faces as stimuli, though data collection using non-face affective stimuli is currently underway. In addition to fMRI data, extensive neuropsychological and psychodiagnostic data were collected, including parent-report data on anxiety.

Results: Data collected to date indicate that increased anxiety is associated with increased amygdala activation during face perception in children in ASD. The relationship appears strongest when considering anxiety dimensionally (i.e., questionnaire measures including the parent-report version of the Screen for Child Anxiety Related Emotional Disorders). The strongest amygdala/anxiety correlations were for panic symptoms and separation anxiety, $r=.30$ and $r=.49$, respectively (p-values of .046 and .001). These correlations remained after removing variance associated with core ASD symptoms (measured via the Social

Responsiveness Scale and the Social Communication Questionnaire).

Conclusions: The present data suggest that increased anxiety is related to amygdala hyperactivity among individuals with ASD. A model is proposed where amygdala activity reflects a hybrid signal of social approach (diminished in ASD) and emotional arousal (heightened among individuals with ASD and co-occurring anxiety). Tests of this model will be greatly facilitated by increased attention paid to mood and anxiety symptoms in ASD, including the development of better diagnostic tools for measuring these symptoms.

129.126 126 Measurement of GABA Brain Metabolites in Children with Autism Spectrum Disorder. W. C. Gaetz^{*1}, L. Bloy², D. J. Wang², R. G. Port², L. Blaskey¹, S. E. Levy¹ and T. P. Roberts¹, (1)*Children's Hospital of Philadelphia*, (2)*The Children's Hospital of Philadelphia*

Background:

¹H-magnetic resonance spectroscopy (¹H-MRS) is a non-invasive neuroimaging technique that allows for estimation of specific in vivo neurochemical metabolites and neurotransmitters such as GABA (γ-amino butyric acid). Numerous post-mortem studies and animal models strongly suggest GABAergic system dysfunction in autism spectrum disorder (ASD). Direct in vivo measurement of GABA has been limited due to technical challenges (e.g. spectral overlap of GABA molecule spectrum with the metabolite Creatine (Cr)). Recently, spectral editing methods such as the MEGA-PRESS technique allow for the separation of GABA from Cr. Presently, a single report has been published using MEGA-PRESS that described GABA downregulation from frontal lobe in children with ASD. This study has yet to be replicated, and it remains unclear whether GABA downregulation observed from one brain area predicts downregulation in other cortical areas.

Objectives:

The objective of the current study was to quantify GABA and Glx measures in a group of (n=17) autistic children (ASD mean age, 11.5 yrs; StDev, 2.65 yrs) and (n=12) typically developing (TD mean age, 12.7 yrs; StDev, 2.64 yrs) children and to attempt to replicate the observation of GABA

downregulation from frontal lobe voxels in ASD. GABA and Cr concentrations were assessed from three separate MRS voxel locations (motor, visual and auditory areas). Thus the secondary objective was to determine whether any observed GABA downregulation in ASD is ubiquitous throughout the brain or is regionally specific.

Methods:

MRI scans were performed with a 3.0 T whole body MR scanner with a thirty-two channel head coil (Siemens Verio). For each participant, a 3D MPRAGE anatomic scan was obtained in an axial orientation (1 mm isotropic voxel resolution; TR/TE=1900/2.87 ms; Inversion time=1100 ms; Flip angle=9°). Single voxel ¹H MRS was measured from 3 separate regions of interest (ROIs): **Motor ROI** (30×30×30 mm): The motor ROI voxel was centered on the "hand-knob" of the left central sulcus. **Visual ROI** (30×30×30 mm): The visual ROI voxel was positioned medially in the occipital lobe, and positioned to avoid including the sagittal sinus and to remain within the occipital lobe. **Auditory ROI** (40×30×20 mm): The auditory ROI voxel was aligned to the left mid-temporal lobe and encompassed the superior temporal gyrus. GABA MRS was obtained using the MEGA-PRESS, with TE=68 ms, T=1500ms and 128 pairs of spectra (acquisition time < 7mins per ROI). Semi-automatic post-processing of spectral signals was carried out using the jMRUI software. GABA quantitation was calculated as the within voxel ratio of GABA to Creatine (Cr).

Results:

The mean GABA/Cr ratio was not significant for Motor or Visual ROIs. However, the GABA/Cr values from Auditory ROIs were significantly lower in ASD relative to TD controls ($p < 0.05$; two-tailed ttest).

Conclusions:

The anticipated GABA decrease from frontal (Motor) ROI was not replicated in our study. However, a significant decrease in auditory GABA/Cr in ASD was observed. This decrease was specific to auditory areas and thus GABA

downregulation appears to be regionally specific feature of the ASD brain.

129.127 127 Altered Prefrontal Activation and Connectivity During Implicit Emotion Judgment in Autism Spectrum Disorders. R. K. Kana*, *University of Alabama, Birmingham*

Background: Judging others' emotions accurately is a critical skill for successful social interaction. Many individuals with autism spectrum disorders (ASD) struggle with everyday social interactions, largely due to difficulty reading others' emotions from faces (Harms et al., 2010; Monk et al., 2010) and from their body postures (Grezes et al., 2009; Hadjikhani et al., 2009). Such difficulty in individuals with ASD may manifest more in implicit assessment of emotions than in explicit situations of emotion attribution. This is relatively under-examined in ASD. This study uses dynamic action scenarios to examine the neural mechanisms, especially the role of inferior frontal cortex (IFC, a key node involved in simulating actions), in mediating implicit and explicit emotion judgment in ASD.

Objectives: The primary objective of this functional MRI study was to investigate the nature of brain responses associated with explicit and implicit perception of emotional information in high-functioning adults with ASD.

Methods: fMRI data were collected from fourteen high-functioning adults with ASD and thirteen typically developing control participants. Participants watched a series of short videos (average 10 seconds long) of characters involved in emotional action scenarios. Participants were told to judge the emotion expressed by the actor (happy, sad, angry, or afraid) or identify a masked object in each video. In control condition, participants watched neutral videos of characters and made a perceptual judgment. The stimuli were presented in an event-related design, and the data were acquired using a Siemens 3T scanner. Data analysis was performed using SPM8.

Results: 1) Behavioral data showed that both groups performed significantly above chance on all video types ($p < .05$), and there were no significant group differences in accuracy or reaction time; 2) There was robust bilateral extrastriate body area (EBA) activation (MNI coordinates: $x = -46, y = -68, z = 0; x = 46, y =$

-66, $z = 0$) in both ASD and typical control participants for both emotion and object tasks; 3) While there was no difference in activation in explicit emotion condition, the participants with ASD showed significantly reduced response in medial prefrontal cortex (MPFC) and right IFC during implicit emotion judgment ($p = 0.005$; cluster size = 80mm^3); and 4) Functional connectivity analysis revealed significant underconnectivity in autism between left IFC and right inferior parietal lobule (IPL) [$t(25) = 2.36$; $p < 0.05$], and between right IFC and left IPL [$t(25) = 2.22$; $p < 0.05$].

Conclusions: Robust EBA activation seen in both groups across conditions suggests intact general perceptual explicit and implicit brain responses to emotional action observation in ASD. However, the limited response in MPFC, and IFC, as well as underconnectivity between IFC and IPL in ASD participants during implicit emotion judgment may suggest their difficulty in reading emotions automatically. It is possible that implicit information may not be associated to its valence in participants with ASD. The activation and functional connectivity data from this study provide valuable insight into understanding bodily emotions in autism.

129.128 128 Abnormal White Matter Microstructure in Posterior Cerebral Tracts Is Associated with Sensory Dysfunction and Impaired Multisensory Integration in Children with Sensory Processing Disorders. J. P. Owen*, E. Fourie, S. Desai, S. S. Hill, J. Harris, P. Mukherjee and E. Marco, *University of California San Francisco*

Background:

Sensory processing disorders (SPD) affect 5-16% of school-aged children and causes long-term deficits in intellectual and social development. Current theories regarding the underlying basis of SPD implicate primary sensory cortical areas and higher-order multisensory integration (MSI) cortical regions. The role of white matter in SPD has not been previously investigated. We hypothesize that reduced microstructural integrity of white matter fibers in primary sensory tracts and/or in tracts projecting to multimodal association areas may result in loss of the precise timing necessary for sensory impulse propagation which serves sensory processing, integration, motor planning and the ability to suppress distracting stimuli.

Objectives:

To test whether microstructural abnormalities of cerebral white matter are associated with sensory dysfunction, impaired MSI, and attention problems in children with SPD using diffusion tensor imaging (DTI).

Methods:

3 Tesla DTI was acquired in 16 boys with SPD and 24 age-, gender-, handedness- and IQ-matched neurotypical controls. All subjects were ages 8-11 years, had full-scale IQ > 70, and a stable medication regimen for over 6 weeks. Auditory, tactile, visual, multisensory, and inattention scores for all subjects were collected using the Sensory Profile, a parent questionnaire. DTI was performed at 2.2-mm isotropic voxel resolution with 64 encoding directions at $b=2000 \text{ s/mm}^2$. FSL was used to calculate fractional anisotropy (FA), mean diffusivity (MD) and radial diffusivity (RD). Nonparametric permutation testing from tract based spatial statistics (TBSS) was used to detect significant group differences in the white matter of the whole brain and to detect regions where DTI parameters were significantly correlated with behavioral variables ($p < 0.05$, corrected for multiple voxel-wise comparisons).

Results:

Significant decreases in FA as well as increases in MD and RD were found in areas of cerebral white matter in the SPD cohort relative to controls, primarily in posterior white matter tracts including the splenium and posterior body of the corpus callosum, the bilateral posterior corona radiata and the bilateral posterior thalamic radiations, including the optic radiations. Significant positive correlations were observed between FA of specific frontal and posterior cerebral tracts and the auditory, multisensory, and inattention scores ($r=0.5-0.7$; $p < 0.001$). Conversely, negative correlations were detected between RD and the multisensory and inattention scores ($r=0.5-0.7$; $p < 0.001$).

Conclusions:

This is the first study to demonstrate reduced white matter microstructural integrity in SPD

patients versus matched controls. We show that DTI microstructural parameters in posterior tracts correlate strongly with sensory dysfunction and abnormal MSI, while left frontal tract integrity correlates specifically with a behavioral measure of attention. These findings suggest abnormal white matter as a biological basis for SPD and also help to establish SPD as a distinct disease separate from overlapping clinical conditions such as autism and ADHD which, at the level of group analysis, have divergent patterns of abnormality on DTI. Using brain-behavior correlations, we hope to move towards a more individualized model for understanding and treating children with sensory processing differences.

129.129 Neural Mechanisms of Improvements in Social Motivation After Pivotal Response Treatment: A Case Series. A. C. Voos*¹, K. A. Pelphrey², C. Cordeaux², L. C. Anderson² and P. Ventola², (1)University of California Santa Barbara, (2)Yale University

Background: Pivotal response treatment (PRT) is an empirically validated behavioral treatment. 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.

The perception of human motion is central to effective social interaction (Blake & Shiffrar, 2007), and disrupted biological motion perception has been documented in children with ASD (Kaiser & Shiffrar, 2009; Kaiser et al., 2010; Klin et al., 2009). Using point light displays of biological motion, a recent fMRI study identified three categories of brain responses (State, Trait, and Compensatory) in a group of typical children (TD), unaffected siblings (US) and children with ASD. Regions reflecting the State of having ASD showed decreased activation in ASD compared to TD and US, Trait regions, reflecting an increased risk for developing ASD, showed decreased activation in children with ASD and US, and Compensatory activity was unique to US.

Objectives: Using a well-established biological motion paradigm (Kaiser et al., 2010), we are able to identify the neural mechanisms utilized

during social perception before and after treatment and identify the neural mechanisms underlying the behavioral improvements resulting from PRT.

Methods: Six children with ASD received 4 months of PRT. Clinical outcome was assessed using the ADOS, CELF-P-2, Vineland-II, and clinical observations of individual behavioral goals. Participants also completed an fMRI scan before and after 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. We constrained our analyses to *a priori* regions of interest (State, Trait and Compensatory) defined using the same task in a prior sample of children (Kaiser et al., 2010). Additionally, participants completed two runs of an eye tracking task, consisting of faces (from the NimStim set) and houses (253 secs).

Results: Preliminary results with two children showed remarkable positive behavioral improvements, as assessed by direct clinician assessment and parent report. In addition, the children showed increased activation in brain regions recruited by typically developing children during social perception. One child showed increased activation in Trait-defined left dorsolateral prefrontal cortex (dlPFC) and two distinct regions of the State-defined left fusiform gyrus (FG). The other child demonstrated greater activation in a portion of the State-defined right posterior superior temporal sulcus (pSTS), State-defined left ventrolateral prefrontal cortex (vlPFC), State-defined right fusiform gyrus (FG) and State/Trait-defined left FG. Eye tracking results were variable, as one child moved towards a more typical visual scanning pattern, while the other child's gaze pattern remained stable.

Conclusions: PRT results in significant gains in social communication skills. fMRI is a highly sensitive and feasible treatment outcome measure and demonstrate that neural systems supporting social perception are malleable in children with ASD.

129.130 DTI Findings Related to Communication Impairment in SLOS. A. Diaz-Stransky*¹, R. W. Y. Lee², E. S. Jung², A. Thurm³ and F. D. Porter⁴, (1)Johns Hopkins University School of Medicine, (2)Kennedy Krieger Institute, (3)National

Background: Smith-Lemli-Opitz Syndrome (SLOS) is an autosomal recessive disorder of cholesterol biosynthesis with a high prevalence of intellectual disability and frequently accompanied autistic behavior and communication deficits. Communication impairment in autism is associated with abnormal hemispheric lateralization and elevated mean diffusivity (MD) in the left superior longitudinal fasciculus (SLF). The relationship between DTI findings in language-associated brain regions and communication impairment in SLOS has not been studied.

Objectives: The aim of this study is to characterize the relationship between DTI findings in language-associated brain regions of interest (ROI) and standardized communication test scores in individuals with SLOS. Outcome measures include MD, mean fractional anisotropy (mFA), and volume of 8 atlas-based ROI. A secondary objective is to report the lateralization indices (LI) of DTI outcome measures in language-associated brain regions.

Methods: Ten children (mean age 10.1 +/-5.5) with SLOS underwent brain imaging on a 3T MRI scanner. Atlas-based DTI data for the right and left inferior frontal gyrus (IFG), superior temporal gyrus (STG), middle temporal gyrus (MTG), and superior longitudinal fasciculus (SLF) were reported using DTI Studio. Communication was assessed with the Vineland Adaptive Behavior Scales (VABS), communication domain (VABS-CD) and the ADI-R, Communication Domain (ADI-R - CD). Laterality Index (LI) = (left - right)/[(left + right)], was calculated for volume and mFA for all four regions. Statistical analysis was performed with student's T-test and Pearson's correlation (r).

Results: In SLOS, lower VABS-CD score is correlated with higher mFA in right SLF ($r=-0.72$, $p=0.023$) and left SLF ($r=-0.77$, $p=0.01$). Higher rate of communication abnormalities according to the ADI-R Communication Domain is correlated with mFA in left STG ($r=0.807$, $p=0.022$), and MD in right SLF ($r=0.723$, $p=0.046$). In terms of laterality index, higher rate of abnormalities, determined by a higher ADI-R-CD correlates with higher mFA LI in the STG ($r=0.61$, $p=0.036$) and

SLF ($r=0.60$, $p=0.038$) and volume LI in the STG ($r=-0.74$, $p=0.006$).

Conclusions: In SLOS, DTI abnormalities in language regions are associated with severity of communication impairment. Specifically, increased lateralization of mFA and volume in the STG is associated with greater severity of communication impairment. Further studies investigating communication impairment in SLOS may lead to a better understanding of the neurobiologic basis of autism and other neurodevelopmental disorders.

129.131 131 On Electrophysiologic and Multimodal Signatures of Language Impairment in ASD. T. P. Roberts*¹, S. Y. Khan¹, K. M. Cannon¹, K. Heiken¹, M. R. Lanza¹, S. Qasmieh¹, K. Hines¹, L. Blaskey¹, D. M. Zarnow², W. C. Gaetz², J. C. Edgar² and S. E. Levy¹, (1)*Children's Hospital of Philadelphia*, (2)*University of Pennsylvania*

Background:

Brain level traits, or endophenotypes, of ASD may serve as diagnostic or prognostic biomarkers. Perhaps more importantly, such brain measures may identify neural systems that lend themselves (1) to patient stratification and thus improve group homogeneity (stratification biomarkers), (2) to measuring therapeutic response, and (3) in translation to the preclinical environment where behavioral analogy is an important, but limited tool.

Objectives:

To draw together results from multiple imaging modalities in a large cohort of children with ASD and both typically developing and clinical controls.

Methods:

Approximately 200 children (6-15yrs) with ASD and age/IQ-matched typically developing (TD) subjects were administered tests of auditory processing while whole-head MEG data were collected. Diagnosis was confirmed via ADOS and ADI-R and/or SCQ. Language impairment was quantified using the Core Language Index (CLI) of the CELF-4. An additional cohort of children with specific language impairment (SLI; language impairment in the absence of ASD) were also recruited. Whole-head biomagnetometer data

(Omega, 275-channel, VSMMedTech Inc.) were obtained during presentation of isolated sinusoidal tones (500 and 1000 Hz) as well as oddball mismatch tone and vowel paradigms. Dependent variables were left and right auditory cortex latencies for M50, M100 and the mismatch field (MMF). MRI (Siemens 3T Verio™) was performed for anatomic registration and for estimation of regional white matter integrity using diffusion tensor imaging (DTI; 30 directions, $b=1000s/mm^2$). In a subset of subjects, levels of GABA in auditory cortex were obtained using the MEGAPRESS MRS sequence (TE=68ms).

Results:

Examining pure tones, M50 and M100 latency were delayed in ASD versus TD. The latency prolongation in ASD persisted even after measures of language impairment (CLI of the CELF-4) and IQ (FSIQ or PRI) were added as covariates. No latency prolongation was observed in the cohort of children with SLI.

MMF latency was prolonged in ASD, especially in the subset of children with ASD with language impairment (CELF CLI < 85). MMF latency was similarly prolonged in children with SLI.

DTI of the acoustic radiations was abnormal in ASD, specifically fractional anisotropy (FA) was reduced and exhibited a flatter developmental trajectory than observed in typical development.

DTI of the left superior longitudinal fasciculus (SLF) was abnormal in ASD, specifically exhibiting elevated mean diffusivity (MD), especially in the subset of children with ASD with language impairment. Although mean diffusivity was also elevated in children with SLI, the most pronounced elevation was observed in the cohort with ASD and language impairment. A 2x2 ANOVA (with factors of ASD/noASD and LI/noLI) with PRI and age as covariates revealed significant main effects ($p<0.05$) of both ASD and LI.

GABA levels in superior temporal gyrus (STG; including auditory cortex) were significantly lower ($p<0.05$) in ASD than TD.

Conclusions:

There is considerable emerging physiologic evidence for brain abnormalities in ASD. Some abnormalities appear to be proportional to clinical severity (in the domain of interest: language).

Converging evidence from multiple modalities supports neurobiological interpretation of developmental anomalies that are both general to ASD and also specific to the language impairment aspect of the phenotype.

129.132 132 Diffusion Tensor Tracking (DTT) of Face Processing

Pathways with Comparison to Sensitive Behavioral Measures: Understanding Microstructure and Detecting Subgroups in Autism. T. E. Conturo^{*1}, D. L. Williams², K. W. Chua³, S. C. Green³, J. R. Mahalchak³, A. R. McMichael¹, C. D. Smith⁴, M. S. Strauss³ and N. J. Minshew³, (1)Washington University, (2)Duquesne University, (3)University of Pittsburgh, (4)University of Kentucky

Background: Children and adults with autism have characteristic impairments in recognizing faces and face emotions. Diffusion tensor tracking (DTT) enables detection/measurement of previously-unknown hippocampo-fusiform (HF) and amygdalo-fusiform (AF) pathways (Smith et.al., 2009), respectively involved in face recognition and emotional processing. Given the importance of face processing in autism, we analyzed HF/AF pathways in adolescents/young adults with autism (Conturo et al., 2008). The right HF pathway (specific for face recognition) had reduced across-fiber diffusivity (D-min). To better understand the microstructural basis for these changes, we compared DTT to sensitive neuropsychological tests (NPTs) of face recognition/emotional processing designed for study of autism. By characterizing participants on two dimensions (2D), participants might also separate into subgroups.

Objectives: Interpret DTT abnormalities and test for subgroups by comparing to sensitive NPTs.

Methods: Custom diffusion-tensor MRI data were acquired in 17 participants with high-functioning autism meeting ADOS/ADI criteria (age 16-53) and 17 controls (individually-matched in age/gender/ethnicity/handedness, and verbal/performance/full-scale IQ). Group differences in right HF D-min ($p=0.014$, paired t-test) were analyzed by administering to 10 of the same autism participants sensitive NPTs of face-gender identification (Wilkinson et.al.,

IMFAR2009) and face-emotion recognition (Rump et al., 2009). Stimulus faces were digitally morphed together to produce subtle gender or emotion (e.g., 40%/60% male/female).

Results: Both the face-gender and face-emotion NPTs showed a strong relation to DTT for both right HF/AF, with slower D-min related to lower performance in all cases. The correlation between D-min and gender identification accuracy was modest ($r=0.42/0.42$ for right HF/AF), with similar results for emotion. A 2D separation of participants into two subgroups was revealed: one subgroup (5 subjects) had low performance with a very low pathway D-min; the other subgroup had higher performance with a slightly higher D-min. Both subgroups exhibited similar DTT-NPT slopes, with very high correlation in the low-performance subgroup ($0.93/0.87$ for right HF/AF). [The high-performance subgroup had lower correlation ($0.33/0.57$).] The consistent association of slower D-min with lower performance indicates that the reduction in right HF D-min in (Conturo et al., 2008) is functionally significant, with the same process likely occurring in right AF. This result is intriguing, as decreased D-min (and a corresponding anisotropy increase) is typically related to higher performance (i.e., more myelination). These results reinforce the microstructural mechanism that we proposed in (Conturo et al, 2008): small-diameter axons in the affected pathways, causing slowed cross-fiber diffusivity and slowed neural transmission. Small diameters could parsimoniously account for the unusual combination of reduced D-min and reduced function. The subgroup analysis suggests that some individuals with less severe diameter reduction can develop mechanisms to achieve normal face processing despite their pathway microstructure. (Such intervening variables likely reduce the correlation in the high-functioning subgroup.) This interpretation is consistent with the known social histories of the participants.

Conclusions: The strong association between decreased D-min and decreased function in face processing pathways supports the mechanism of small-diameter axons in autism. Sensitive DTT measures of autism-relevant pathways, combined with sensitive NPT measures of pathway function, has potential to elucidate autism mechanisms and reveal autism subtypes.

129.133 133 Cortical Thickness Changes in Autism Spectrum Disorders Associated with Age and Social Cognitive Behaviours. K. A. R. Doyle-Thomas^{*1}, N. E. Foster², A. Tryfon², T. Ouimet³, K. L. Hyde⁴, A. C. Evans², L. Zwaigenbaum⁵, E. Anagnostou⁶ and .. NeuroDevNet ASD Imaging Group⁷, (1)*Bloorview Research Institute*, (2)*McGill University*, (3)*Montreal Children's Hospital Research Institute*, (4)*Montreal Neurological Institute, McGill University*, (5)*University of Alberta*, (6)*University of Toronto*, (7)<http://www.neurodevnet.ca/research/asd>

Background: There is considerable evidence of atypical brain volume development in individuals with Autism Spectrum Disorders (ASD). However, little is known about how maturational changes in aspects of cortical morphology, such as cortical thickness contribute to these atypicalities, and how changes relate to diagnostic features of ASD, such as social impairment.

Objectives: We examined (1) developmental changes in cortical thickness in ASD individuals and typically developing controls, (2) the relation between cortical thickness and Reading the Mind in the Eyes scores between groups, and (3) in the ASD group, the relation between cortical thickness and social scores on the Autism Diagnostic Interview-Revised (ADI-R).

Methods: Structural Magnetic Resonance Imaging (MRI) scans were obtained from 64 participants, between the ages of 7-17 years. Groups had significantly different IQ scores (ASD: 96.69 ± 17.89 and TD: 115.87 ± 9.58 , $p < 0.05$). Based on available data, we included the following number of participants in each analysis: aim (1) 28 ASD and 36 controls, aim (2) 27 ASD and 30 controls and aim (3) 12 ASD. These preliminary analyses were carried out using general linear models, controlling for sex in all analyses, and additionally controlling for age in aims 2 and 3.

Results: Age-related, cortical thickness differences between groups were observed in middle, medial and superior frontal regions, as well as the precuneus and cuneus. An interaction between thickness and Reading the Mind in the Eyes scores were found in frontal regions (middle, cingulate), parietal regions (precuneus, postcentral) and an inferior temporal region. Lastly, an association was observed between thickness and symptomatology, with poorer social

scores on the ADI-R being associated with thicker cortices in the middle and medial frontal gyri.

Conclusions: These results show several examples of cortical thickness atypicalities and how it may contribute to social impairments. Age-related thickness differences in frontal brain regions may contribute to known developmental brain volume atypicalities in ASD. Similarly, the relation between thickness changes in the middle and medial frontal gyri, as well as the fusiform gyrus, and atypical social behaviour is consistent with activation differences in these regions during social emotion tasks. Thus, the findings of the present study suggest that cortical thickness atypicalities are present in ASD and relate to social impairments in ASD.

129.134 134 Abnormal Connectivity in the Social Brain in ASD Identified Via Naturalistic Social Perception and Independent Components Analysis. D. Giovannelli¹, J. E. Letzen², R. T. Schultz³ and J. D. Herrington*⁴, (1)*Haverford College*, (2)*University of Florida*, (3)*Children's Hospital of Philadelphia*, (4)*University of Pennsylvania*

Background: There is substantial evidence that ASD is associated with functional abnormalities in the "social brain", including amygdala, medial prefrontal cortex, fusiform gyrus, and superior temporal sulcus. Although most studies on the social brain in ASD treat each of these areas in isolation, findings of abnormal white matter development in ASD suggest that social perception deficits may have as much or more to do with diminished communication between structures as abnormalities within them. The present fMRI study examines connectivity between nodes of the social brain via two underutilized methodological approaches. The first involves the perception of naturalistic social videos with no specific task instructions (passive viewing), in order to maximize the possibility of observing network-wide (as opposed to task and region-specific) activation. Participant attention was monitored via simultaneous eyetracking and an unanticipated post-scan quiz on the content of the videos. The second was the use of spatiotemporal independent components analysis (ICA) – an approach that is sensitive to coordinated patterns of activation across networks.

Objectives: This study tests for abnormal connectivity between nodes of the social brain in ASD during naturalistic social perception.

Methods: ASD and typically developing control (TDC) samples were scanned for 8.2 minutes while they watched videos of two children playing. Videos alternated between 1-minute depictions of two children playing together (joint play) or separately (parallel play). Data collection is ongoing, with the present sample consisting of 27 ASD and 37 TDC participants. ASD diagnoses were established via ADOS and ADI-R. Groups were matched on age (ASD=10.0, TDC=9.3) and cognitive ability (Differential Abilities Scale-II GCA, ASD=108, TDC=112). Independent components were identified by combining both TDC and ASD groups, then testing for post hoc differences in component weighting as a function of group and task condition (joint versus parallel play). ICA was carried out for two separate subsets of participants (each including TDC and ASD) who received two different counterbalanced block orders; the first order was used to identify independent components, and the second was used to replicate them.

Results: A single spatiotemporal independent component was identified spanning amygdala, medial prefrontal cortex, fusiform gyrus, and periamygdala. Weightings for this component were significantly greater for the joint than the parallel play condition ($p < .001$), suggesting that the network is modulated by the amount of social information in a scene. Although the component was identified by pooling data from ASD and TDC groups, weightings for this component were significantly less in the ASD than the TDC group ($p = .039$), indicating abnormal network connectivity in ASD. Analyses integrating eyetracking data with these fMRI results are ongoing.

Conclusions: Findings from this study indicate that social perception deficits in ASD may arise from deficits in connectivity between nodes of the social brain. These findings are particularly compelling, as they rely on a statistical procedure (ICA) that makes no a priori assumptions about functional task (joint versus parallel play) or group (ASD versus TDC), and yet can distinguish both.

129.135 135 Brain and Behavioral Correlates of Auditory-Motor Synchronization in Children with Autism Spectrum Disorder. A. Tryfon*¹, N. E. Foster¹, T. Ouimet², K. A. R. Doyle-Thomas³, E. Anagnostou³, A. C. Evans¹, L. Zwaigenbaum⁴, K. L. Hyde¹ and .. NeuroDevNet ASD Imaging Group⁵,
(1)*Montreal Neurological Institute, McGill University*,
(2)*Montreal Children's Hospital, McGill University*,
(3)*Holland Bloorview Kids Rehabilitation Hospital*,
(4)*University of Alberta*,
(5)<http://www.neurodevnet.ca/research/asd>

Background: Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by deficits in social and communication skills as well as repetitive behaviors and restricted interests.

The "mirror-neuron system" (MNS) refers to a group of neurons that fire when performing an action as well as observing that same action performed by another. Studies in vision point to an atypical functioning of the MNS in individuals with ASD versus typical development (TD). A parallel MNS-like system is thought to exist in the auditory domain in the context of auditory-motor synchronization (Chen et al., 2008). As in vision, recent evidence suggests that MNS regions may also be affected in the auditory domain in ASD (Wan et al, 2010). However, no one has examined basic auditory-motor synchronization in ASD versus TD children.

Objectives: The objectives of the present research were: 1) to test for group differences between ASD and TD children on a basic auditory-motor synchronization task, and 2) to investigate the correlation between performance on this task with brain structure.

Methods: We present preliminary data from 27 ASD and 40 TD control children as part of the 'NeuroDevNet ASD project', an ongoing multi-site study on brain and behavioral development in ASD. The groups were matched on age (from 6-16 years old), and all subjects had an IQ above 70. In an auditory-motor synchronization task, subjects were asked to tap in synchrony with auditory rhythms of varying levels of complexity (easy, simple, and complex). We acquired T1-weighted MRI anatomical scans from all children on a 3T scanner. We performed cortical thickness (CT) analyses on these MR data and then correlated performance on the auditory-motor task with the CT results. Ethical approval for this research was obtained by the Montreal

Neurological Institute and Hospital Research Ethics Board.

Results: Preliminary results revealed that all children (both ASD and TD) performed worse on more complex rhythms. However, children with ASD showed better performance relative to TD on the most complex rhythms. In TD, performance on the auditory-motor task was negatively correlated with CT in motor cortex. In contrast, ASD individuals showed a positive correlation between performance and CT in motor cortex.

Conclusions: We provide preliminary brain-behavioral evidence that basic auditory-motor synchronization might be enhanced in children with ASD relative to TD. Our cortical structure analyses signal potential alterations in the 'auditory MNS' system in ASD. These findings are in contrast to the view that ASD individuals are generally impaired in cross-modal processing. However, these findings are consistent with current models of enhanced basic (low-level) processing in ASD.

129.136 136 Autism Traits in the Typical Population Are Related to Regional Changes in Brain Structure. L. Gebauer*¹, N. E. Foster², P. Vuust³ and K. L. Hyde⁴, (1)*Center of Functionally Integrative Neuroscience, Aarhus University*, (2)*McGill University*, (3)*The Royal Academy of Music, Denmark*, (4)*Montreal Neurological Institute, McGill University*

Background: Autism spectrum disorder (ASD) is characterized by impaired social interaction and communication, and repetitive behaviors.

However, these traits are highly variable across individuals with ASD. Some have argued that ASD forms a continuum, which extends into the general population. Recent work has shown that the extent to which typically developed (TD) adults display autistic traits, as measured using the autism-spectrum quotient (AQ) (Baron-Cohen et al., 2006), predicts performance on behavioral tasks that are impaired in ASD (e.g. social cognition and communication). However, only two studies have examined the structural brain correlates of the AQ in TD, and no study has investigated the correlation between brain structure and the AQ in both TD and ASD.

Objectives: The objective of the present study was to investigate whether differences in autistic traits, as measured with the AQ, are related to

regional brain structure in a similar way in both TD and ASD adults.

Methods: Participants included 26 adults with ASD (mean age= 28.9, *SD*= 6.8, mean IQ = 109.73, *SD*= 13.6) and 26 typically developing adults (mean age = 25.2, *SD*= 4.4, mean IQ = 115.96, *SD*= 11.6). All participants completed the AQ.

T1-weighted structural MR images were obtained for all participants on a 3T MRI scanner. Detailed gray matter measures were performed using cortical thickness analyses via the CIVET pipeline.

We then performed correlations between the total AQ score and the cortical thickness results to test for possible interactions across the ASD and TD groups.

Results: As expected, the ASD group scored higher than the TD group on the AQ overall.

Preliminary analyses revealed an inverse relationship between total AQ score and cortical thickness in inferior frontal and precentral gyrus in both ASD and TD. However, only the TD group (and not ASD) showed a positive correlation between total AQ score and cortical thickness in parahippocampal gyrus.

Conclusions: These preliminary results are consistent with previous findings of atypical brain structure and function in frontal cortex that was related to atypical social cognition in ASD. We provide evidence that autistic traits are reflected in specific brain structures across TD and ASD in a partially overlapping way.

Treatment Trials: Behavioral Interventions Program

130 Treatments: Interventions in School Age, Adolescents and Adults and Social Skills Interventions.

this session has posters describing interventions for older children and adults as well as social skills interventions.

130.137 137 Skills for Living: Evaluation of a Skill-Training Group for Adults with Autism Spectrum Disorders. J. Montgomery*¹, S. North², B. M. Stoesz¹ and K. Carpick¹,
(1)University of Manitoba, (2)Pembina Trails School Division

Background: Individuals with autism spectrum disorders (ASD) experience severe and ongoing difficulties interacting with others and have problems developing and maintaining relationships. These difficulties persist and may even increase in adulthood, yet support services are rarely accessible. Skill training can help adults with ASD learn to cope with a wide range of

social, workplace, and everyday situations, develop meaningful and lasting relationships, and create structure in their lives that will enable them to live healthier, happier, and more fulfilling lives.

Objectives: We developed a consumer-driven skill-training program that aimed to meet the expressed needs of adults with ASD living in Manitoba. Curriculum developed included cognitive behavioural approaches combined with explicit skill teaching, emphasis on practice and skill generalization, and a client-driven approach to topic/goal selection. Moreover, self-understanding was a critical goal of sessions.

Methods: Groups consisted of 8-10 adults with ASD who were not receiving other means of support. Prior to the beginning the program participants were interviewed to determine specific areas of need, personal interests, and goals for personal development. The program curriculum included such topics as: understanding your own and others' emotions, non-verbal cues and body language, dealing with frustration and anxiety, building and maintaining friendships and romantic relationships, and employment skills. Each lesson involved facilitator-lead discussions, role-playing scenarios, and various small and large group activities. Before and after the program, participants completed the Emotional Quotient Inventory - Short Version (EQ:iS) and the Quality of Life Inventory (QOLI) to assess emotional development and implications for everyday living. Moreover, some participants provided comments and feedback about the program.

Results: Results indicated that scores on EQ:iS improved from pre- to post-group participation. QOLI scores were in the 'Low' range prior to the program, and satisfaction ratings in various domains targeting by the curriculum increased after participation. Comments from participants indicated that they believed the program was beneficial and they hoped to take part in further programming of this kind.

Conclusions: Consumer-driven programs can be used to improve intrapersonal and interpersonal emotional intelligence and quality of life, while also providing adults with ASDs with input into their own programming that is respectful and meaningful. While this approach is promising,

evaluation also points to ongoing concerns for adults with ASDs. Specifically, while quality of life improved with intervention, reported levels are still significantly lower than typically developing individuals, and areas that individuals with ASDs rate as important (e.g. Love) are not often explicitly addressed in programming. It is essential to provide programming for adults on the spectrum that is respectful of their own goals and needs, particularly in light of the paucity of supports in adulthood.

130.138 138 PEERS® for Young Adults: Predictors of Social Skills Treatment Outcome in Young Adults with Autism Spectrum Disorders. J. Hopkins*¹, R. Ellingsen², S. Bates³ and E. Laugeson⁴, (1)UCLA PEERS Clinic, (2)University of California Los Angeles, (3)UCLA PEERS Program, (4)UCLA Semel Institute for Neuroscience & Human Behavior

Background:

Autism Spectrum Disorders (ASD) constitute a group of disorders characterized by core deficits in communication, social reciprocity, and overall social functioning that are developmentally pervasive. In particular, young adults with ASD present with difficulties in sustaining interpersonal relationships, romantic interactions, and navigating social environments as a result of deficient social skills (Kanne et al., 2009). While social skills training is a common and important method of treatment, identifying factors that predict treatment outcome is also essential to the development and evolution of social skills interventions designed for young adults with ASD. The Program for the Education and Enrichment of Relational Skills (PEERS®) is an evidence-based and caregiver-assisted intervention that targets the core social deficits of ASD and fosters essential relationship skills for high-functioning young adults on the spectrum. Research examining the effectiveness of PEERS® for Young Adults has revealed significant enhancements in social engagement, communication, and overall social functioning (Gantman et al., 2012); however, predictors of treatment outcome have yet to be examined. In particular, the impact of baseline social functioning and empathy on treatment outcomes among young adults with ASD has yet to be investigated.

Objectives:

The present study examines the relationship between baseline social responsiveness and self-reported empathy on multi-dimensional social treatment outcome measures among young adults with ASD following the completion of a 16-week caregiver-assisted social skills intervention.

Methods:

Twenty-seven young adults with ASD ranging from 18-28 years of age ($M=20.9$, $SD=2.35$) and their caregivers participated in weekly 90-minute group treatment sessions for 16 weeks as part of the PEERS® for Young Adults social skills intervention. Group participants completed various pre and post-intervention measures including the Social Responsiveness Scale (SRS; Constantino, 2005), Empathy Quotient (EQ; Baron-Cohen & Wheelwright, 2004), and the Quality of Socialization Questionnaire-Young Adult (QSQ-YA; Frankel & Mintz, 2008), the latter of which assesses the frequency of social interactions through initiated and invited get-togethers and dates. Baseline SRS and EQ scores were examined to understand the relationship between pre-treatment caregiver-reported social responsiveness and young adult self-reported empathy with post-treatment outcome, as measured by improvement in frequency of social interactions with peers on the QSQ-YA.

Results:

Results indicate that baseline caregiver-reported SRS total scores significantly predict increased frequency in the total number of peer social interactions as measured by the QSQ-YA ($p<.05$) post-treatment. In particular, results reveal that baseline SRS total scores significantly predict change in young adult initiated get-togethers ($p<.05$) and dates ($p<.05$), as well as invited dates ($p<.05$). Likewise, baseline self-reported EQ total scores significantly predict increased frequency of young adult initiated dates ($p<.05$), as well as invited dates ($p<.05$).

Conclusions:

Results suggest that following the completion of the PEERS® for Young Adults intervention, baseline caregiver-reported social responsiveness predicted treatment outcome for frequency of

social interactions among young adults with ASD, including both platonic and romantic relationships. Furthermore, baseline young adult self-reported empathy appears to predict treatment outcome specific to the frequency of romantic interactions post-intervention.

130.139 139 Bullying in Adolescents with Asperger Syndrome: Clinical and Therapeutic Aspects. F. Pourre*, J. Andanson, E. Aubert and J. P. Raynaud, *CHU de Toulouse*

Background: Adolescents with Asperger syndrome are frequently bullied. This led to an increase in social difficulties, anxiety and behavior disorders, school phobias or depressive episodes.

Objectives:

- To describe this phenomenon in 42 adolescents with Asperger syndrome participating in social skills groups.

- To define strategies carried out in social skills groups to help teens suffering from bullying.

Methods:

We systematically collected information regarding bullying in 42 adolescents participating in social skills groups. Data were analyzed: source, frequency and type of bullying, context and mode of revelation, behavioral, emotional and cognitive consequences in teenagers, impact on family and applied measures.

From this information, we developed a specific module based on Cognitive Behavioral Therapy for prevention and management of bullying. Integrated into social skills groups program it can be completed, as required, by a specific action. These strategies include a partnership with parents and schools. We will illustrate this form of intervention by clinical examples.

Results: 90% of adolescents participating in social skills groups relate experiences of bullying such as teasing, insults, threats, manipulation, cyberbullying or physical violence. In more than two-thirds of cases of bullying, the social skills groups integrating a specific module for prevention and management of bullying can remove or significantly reduce this phenomenon.

In addition there is significant improvement in scales of social reciprocity (Social Responsiveness

Scale), theory of mind (Faux pas recognition test), friendship (Friendship questionnaire) and anxiety (Revised Child anxiety Depression Scale).

The prospects for improving the methodology and limitations of strategies implemented are described and discussed. Hypotheses about the specificity of bullying in adolescents with Asperger syndrome are proposed.

Conclusions: The importance of bullying in children and adolescents with Asperger syndrome involves actions of information and intervention with parents and schools as well as the development of specific strategies through social skills groups. Our results, together with data from the international literature suggest practical means of preventing and coping for adolescents with autism spectrum disorders who are victims of bullying.

130.141 141 A Comparative Effectiveness Trial of a School- and Home-Based Executive Functioning Intervention Versus a Social Skills Intervention; Part One: Contextual Effects. L. G. Anthony*, L. Cannon², J. F. Strang¹, M. Wills¹, C. Luong-Tran¹, J. L. Sokoloff¹, E. Bal¹, M. A. Werner², K. C. Alexander², K. K. Powell¹, A. C. Sharber¹, M. Rosenthal³, G. L. Wallace⁴ and L. Kenworthy¹, (1)*Children's National Medical Center*, (2)*Ivymount School*, (3)*Child Mind Institute*, (4)*National Institute of Mental Health*

Background:

Difficulties with executive functioning (EF) are a commonly observed associated feature of ASD. We have developed a school-based group intervention to improve flexibility, goal-setting and planning in students with ASD, the *Unstuck and On Target* intervention (UOT; Cannon et al, 2011). UOT emphasizes real world interventions to remediate EF deficits through cognitive training, self-regulatory scripts, practice and cueing with visual supports in classroom and home settings. UOT teaches what flexibility is and why it is important, how to be flexible, goal-setting, planning and coping skills.

Objectives:

To evaluate the effectiveness of this new intervention, we compared children's social and EF skills before and after participation in either social skills training (SS) or UOT. The comparison

intervention used selections from Baker's (2003) Social Skills curriculum. To aid generalization, both groups were contextually-based (school), with classroom teacher and parent training to extend the skills in multiple contexts.

Methods:

The interventions were embedded in 14 mainstream elementary schools (12 public, 2 parochial) that serve students with ASD through inclusion. All children had IQ>70 (mean=108), met criteria for ASD on ADOS or ADI and clinician impression, and were in 3rd-5th grade. Children were randomly assigned to UOT (N=47) or to SS (N=20). The groups were well-matched on age, sex, type of school, parent education level, IQ, percent on psychotropic medication and race/ethnicity (35% minority/10% Hispanic/Latino). Both interventions were delivered by school staff to small groups of students in at least 27 sessions of 30-40 minutes each. The two interventions were matched for "dose" of intervention and amount of parent, teacher and interventionist training.

Contextual data were collected via classroom observations as well as parent and teacher questionnaires (Social Responsiveness Scale, Behavior Rating Inventory of Executive Functioning Shift and Plan/Organization Subscales). Observer's fidelity ratings of the groups indicated high fidelity overall. There were some problems with cross-condition contamination, however, with some in the SS group having exposure to the UOT intervention. We compared change from pre- to post-intervention via repeated measures ANOVA and post-hoc paired samples t-tests. For each significant interaction, Cohen's d is also presented as an estimate of effect size, as the group Ns were unequal.

Results:

Children in both groups improved with intervention in many areas, but children who participated in UOT groups improved more in flexibility as rated by both their classroom teacher (time*group $F=8.82, p<.01$; Cohen's $d=.62$), and parents (time*group $F=5.23, p<.05$; $d=.58$), and parents noted that flexibility problems caused less

interference (time*group $F=4.02, p<.05$; $d=.51$). UOT students also made greater improvements in the classroom as rated by an independent observer: they were better able to compromise ($x^2=6.96, p<.01$), follow rules ($x^2=11.41, p<.001$), transition from one activity to another ($x^2=15.75, p<.001$), resist getting stuck ($x^2=6.38, p<.05$), and they expressed less negativity ($x^2=3.74, p=.05$). There was no significant difference in the improvement between the SS and UOT groups in social reciprocity ($x^2=1.76, ns$) or classroom participation ($x^2=2.47, ns$).

Conclusions:

These data point to the real-world effectiveness of a contextually-based EF intervention over and above social skills training for children with ASD and without ID.

130.142 142 Effect of PEERS Intervention On Self-Esteem and Self-Concept in Adolescents with ASD. J. Wasisco*, A. V. Van Hecke, J. S. Karst, S. Stevens, K. A. Schohl, B. Dolan, R. J. Remmel, N. Fritz, G. McDonald, J. Kahne and A. Reveles, *Marquette University*

Background: Self-esteem is associated with many aspects of adolescent mental health, including relationship satisfaction, affect, and mood (Orth, 2012). However, few studies have investigated self-esteem in adolescents with Autism Spectrum Disorders (ASD). Lifelong social impairment likely impedes self-esteem development in children with ASD. Therefore, evaluation of interventions should include assessment of this construct. The Program for the Education and Enrichment of Relationship Skills (PEERS; Laugeson & Frankel, 2009) is an evidence-based, social skills intervention for adolescents with ASD. Though several studies have observed positive outcomes for teens following PEERS, there is little research discussing the impact of PEERS on self-esteem.

Objectives: The purpose of this study is to understand how involvement in PEERS intervention affects teenagers with ASD in terms of self-esteem and self-concept. Additionally, we explored the relationship between self-esteem and related constructs including social anxiety and cognitive functioning.

Methods: Thirty-five teenagers with ASD were randomly assigned to an "Experimental" (n = 20) or "Waitlist Control" group (n = 15) prior to PEERS intervention. Prior to intervention, both groups were administered several measures including; The Autism Diagnostic Observation Schedule-General (ADOS-G), Kaufman Brief Intelligence Test-Second Edition (KBIT 2), and Piers-Harris Children's Self-Concept Scale-Second Edition (Piers & Herzberg, 2002). The "Experimental" group then participated in weekly 1.5 hour sessions of PEERS over the course of 14 weeks. Both groups were then reassessed on the Piers-Harris scales immediately following treatment.

Results: A two-way, mixed between-within group Analysis of Variance (ANOVA) was performed to examine the impact of PEERS on overall self-esteem as well as specific components measured by the Piers-Harris, including: behavioral adjustment, intellectual and school status, physical appearance, freedom from anxiety, popularity, and happiness and satisfaction. The group by time interaction was not statistically significant for any of the variables of interest. However, there was a statistically significant main effect for popularity for both the Experimental and Waitlist groups $F(1, 33) = 4.15, p = .05$, with a larger mean change found in the Experimental group. Additionally, bivariate correlational analyses indicated a medium positive correlation between self-esteem change and social impairment on the ADOS, $r = .379, n = 35, P = .025$, with greater initial social impairment associated with greater change in self-esteem. In the experimental group, there was a positive correlation between Full Scale IQ score on the KBIT and change in self esteem, $r = .436, n = 20, p = .054$.

Conclusions: Results did not suggest an overall change in self-esteem in adolescents with ASD following PEERS intervention over and above changes in a waitlist control group. However, there was a significant main effect for popularity, suggesting that teens with ASD did feel more accepted by same-aged peers following intervention. Results may have been limited by sample size, and it is important to further explore this question with a larger sample size. In addition, correlational analyses suggested that greater impairment in social behavior prior to

PEERS actually contributed to more change in self-esteem.

130.143 143 A Randomized Controlled Trial of the Korean Version of the PEERS® Parent-Assisted Social Skills Training Program for Teens with ASD. H. J. Yoo*¹, E. Laugeson², G. Bahn³, I. H. Cho⁴, E. K. Kim⁵, J. H. Kim⁶, J. W. Min⁷, W. H. Lee⁷, S. S. Jun⁵, J. S. Seo⁸, G. Y. Bong¹, B. N. Kim⁹ and S. C. Cho¹⁰, (1)Seongnam Child and Adolescent Community Mental Health Center, (2)UCLA Semel Institute for Neuroscience & Human Behavior, (3)Kyung Hee University School of Medicine, (4)Gacheon University of Medicine and Science, (5)Dankook University, (6)Seoul National University Bundang Hospital, (7)Kyung Hee University Medical Center, (8)Gacheon University Ghil Hospital, (9)Seoul National University College of Medicine, (10)Seoul National University Hospital

Background: Impaired social functioning is a hallmark feature of Autism Spectrum Disorders (ASD), often requiring treatment throughout the lifespan. PEERS® (Program for the Education and Enrichment of Relational Skills) is a parent-assisted social skills training for teens with ASD (Laugeson and Frankel, 2010). Although PEERS® has an established evidence-base in improving the social skills of adolescents (Laugeson et al., 2009; 2012) and young adults (Gantman et al., 2012) with ASD in North America, the efficacy of this treatment has yet to be established in cross cultural validation trials.

Objectives: The objective of this study is to examine the feasibility and treatment efficacy of a Korean version of PEERS® for enhancing social skills through a randomized controlled trial.

Methods: The English version of PEERS® Treatment Manual (Laugeson & Frankel, 2010) was translated into Korean and reviewed by 21 child mental health professionals. Items identified as culturally sensitive were surveyed by 445 middle school students and material were modified accordingly. Participants included 41 teens between 12-18 years of age with a previous diagnosis of ASD and verbal IQ ≥ 70 . ASD diagnosis was confirmed using the ADOS (Lord et al., 2003) and the ADI-R (Lord et al., 1994). IQ and adaptive functioning were assessed using the KEDI-WISC (Park et al., 1991) and K-VABS (Kim & Park, 1992). Eligible teens were randomly assigned to a Treatment Group (TG; $n=23$) or Delayed Treatment Control Group (CG; $n=18$). TG participants completed outcome measures on the

first and last session of the intervention, while CG participants completed outcome measures upon entering the study, and at the first and last session of the treatment. Primary outcome measures included the ADOS, K-VABS, Social Skills Rating System (SSRS; Gresham & Elliot, 1990), and Test of Adolescent Social Skills Knowledge (TASSK; Laugeson & Frankel, 2010). Secondary outcome measures included scales for depression and anxiety.

Results: There were no significant differences in age (14.04 ± 1.64 & 13.78 ± 1.48 years), IQ (99.26 ± 15.38 & 99.28 ± 18.60), parental education, SES, or autism symptoms between groups ($p > .05$). Treatment efficacy was analyzed by ANCOVA, controlling pre-treatment scores as covariates. Results suggest that the TG showed significant improvement in Interpersonal Relationship and Play/Leisure Time on the subdomain scores of K-VABS (p 's < 0.01) and total scores of the TASSK ($p < 0.01$) following treatment. The TG also showed significant improvement in Language and Communication and Reciprocal Social Interaction Domain scores on the ADOS (p 's < 0.01) following intervention. Secondary outcome analyses reveal weak but significant differences in state anxiety in the two groups after intervention ($p = 0.045$), and a significant decrease in maternal state anxiety in the TG after controlling for baseline level ($p < 0.01$).

Conclusions: Despite cultural and linguistic differences, the PEERS[®] social skills intervention appears to be efficacious for teens with ASD in Korea with modest cultural adjustment. In a randomized controlled trial, participants receiving the PEERS[®] treatment showed significant improvement in social skills knowledge, interpersonal skills, play/leisure skills, and state anxiety, as well as a decrease in autism symptoms. This study represents one of only a few cross-cultural validation trials of an established evidence-based treatment for adolescents with ASD.

130.144 144 Research in Action - an Evaluation of the Secret Agent Society Social Skills Program in a Specialist School Context. R. B. Beaumont^{*1}, K. Sofronoff², K. M. Gray³, J. R. Taffe³, T. Clark⁴, D. M. Costley⁴, A. Redoblado Hodge⁵, J. Roberts⁶, S. K. Horstead⁷, K. Clarke⁷ and S. L. Einfeld⁷, (1)*Social Skills Training Institute*, (2)*School of Psychology, University of*

Queensland, (3)*Monash University*, (4)*Autism Spectrum Australia (ASPECT)*, (5)*The Children's Hospital at Westmead*, (6)*Autism Centre of Excellence, Griffith University*, (7)*University of Sydney*

Background: Social skill deficits are a core diagnostic feature of children with Autism Spectrum Disorders (ASDs). They include difficulties identifying and expressing emotions in appropriate ways, troubles initiating and maintaining conversations, challenges in engaging in interactive play and problems making and keeping friends. These social difficulties are most apparent at school, where teachers face the challenging task of supporting the social and emotional needs of students on the spectrum. As one of the world's largest providers of autism-specific education, Aspect (Autism Spectrum Australia) sought to evaluate whether augmenting their existing primary- and high-school satellite class curriculum with a multimedia social skills program (The Secret Agent Society) would lead to better outcomes for their students with ASDs.

Objectives: This study aimed to evaluate whether the Secret Agent Society Program was effective in improving students' social skills at home, at school and their peer interactions during classroom activities. It also aimed to evaluate whether the program resulted in sustained improvements in students' social functioning at 6- and 12-month follow-up.

Methods: Eighty students aged 8.2 to 14.6 years who attended Aspect specialist classes for students with ASDs across five school districts participated in the study. The Wechsler Abbreviated Scale of Intelligence and Peabody Picture Vocabulary Test-4 were used to assess children's intellectual and receptive language abilities respectively. Students were eligible to participate in the trial if they attended a school involved in the research and were aged between 8 and 15 years at the commencement of the study.

Students were assessed on parent-report, teacher/teacher-aide report, child competency and observational assessment measures of emotion recognition, emotion regulation and/or social skills at the beginning and end of a baseline period (approximately 2 months) where they engaged in the usual school curriculum. They then participated in the Secret Agent Society Program

– a 10 week intervention consisting of a computer game, weekly child therapy sessions (each 90 minutes in duration), 4 x two-hour parent sessions, weekly teacher tip sheets and three- and six-month booster sessions. The program uses visual resources and fun games to teach children how to recognise emotions in themselves and others, manage feelings of anxiety and anger, talk and play with others, detect the difference between friendly joking and mean teasing and cope with bullying. The manualised program was delivered to groups of three to six students by one or two trained facilitators (typically their classroom teachers). Assessment measures were readministered at the end of the program, and at 6- and 12-months follow-up.

Results: Results from hierarchical linear modelling analyses will be presented that evaluate the relative gains in social functioning made by students over the intervention and baseline periods. Six-month and 12-month follow-up data will also be reviewed to determine durability of treatment gains, together with data identifying factors that distinguished treatment responders from non-responders.

Conclusions: Results from this study provide support for the effectiveness of delivering the Secret Agent Society Program within a school context. Limitations of the study will be discussed, together with recommendations for school-based delivery of social skills programs to students with ASDs.

130.145 Observation of Peer Engagement in a Peer Mediated Intervention Model for Adolescents with ASD. F. Orlich^{*1}, R. Oti¹, K. M. Burner¹, R. Montague¹, R. Poole¹, R. Bernier², B. H. King³, C. Lord⁴ and C. Kasari⁵, (1)Seattle Children's Research Institute, (2)University of Washington, (3)University of Washington and Seattle Children's Hospital, (4)Weill Cornell Medical College, (5)University of California Los Angeles

Background: Adolescents with ASD report poorer peer relationships, fewer friends, and greater loneliness than their typical age classmates (Bauminger & Kasari, 2000; Chamberlain, Kasari & Rotheram-Fuller, 2007). Current efforts are focused on improving social skills and peer relationships in adolescents through social skills interventions. Thus far, most of these studies have relied on self-report and parent-report data to measure outcome which may be subject to bias

or inaccuracy (Tantam 2000). There is limited availability of naturalistic observational measures to capture change in peer engagement in response to these interventions.

Objectives: The main objective of the current study was to determine if observation of teen engagement changed after implementation of a school-based peer mediated model of intervention.

Methods: Adolescents with ASD were randomized into either a social skills treatment delivered in a didactic learning style with emphasis on practice of rote skills (SKILLS, $n = 16$) or a peer mediated model of teen engagement (ENGAGE, $n = 18$). Treatment consisted of 8 weekly sessions held after school or during lunch in the school. The Teen Observation of Peer Interaction (TOPI) is a behavioral observation measure that allows for observation of peer interactions (e.g., proximity to peer, level of complexity in social engagement with another peer). The TOPI consists of five 90-second observation intervals and rates "engagement state" from "solitary" to "joint" on a six point scale for each interval. The TOPI was administered during school lunches at pre-intervention, post-intervention, and at 8-12 weeks after the end of intervention. Observers of teen engagement were naïve to intervention type status and time point. An overall average engagement state was calculated at each time point.

Results: There were no differences in observed levels of peer engagement between groups prior to intervention. At post-intervention, adolescents in the ENGAGE intervention were rated significantly higher on levels of peer engagement compared to the those in the SKILLS intervention ($F(1,31) = 4.11, p = .05$) (ENGAGE: $M = 3.74, SD = 1.75$; SKILLS: $M = 2.63, SD = 1.35$). Although there was no significant difference between groups at 8-12 week follow up, the ENGAGE group continued to have higher engagement scores than at pre-intervention.

Conclusions: Results suggest that adolescents in the ENGAGE model participated in more complex peer social interactions post-intervention compared to adolescents in the SKILLS model. Although there were no differences between groups at follow-up, improvement in social

engagement in the ENGAGE group was maintained from end of treatment to follow-up. It may be that adolescents participating in the ENGAGE intervention exhibited greater peer engagement due to more opportunity for social interactions with other peers in the group. Participants in the ENGAGE group were encouraged to speak to each other outside of group, and social engagements were frequently planned ahead of time. This type of structured approach to increasing engagement between teens with ASD and their peers may have been important for teaching teens to alter their social "routine."

130.146 146 Guiding Children with High-Functioning Autism Through Early Life Transitions: New Approaches. O. Baykaner*¹, S. Anderson², S. M. Staunton³, J. Hellriegel⁴, M. Murin⁵, W. Mandy⁶ and D. H. Skuse³, (1)*Institute of Child Health*, (2)*Great Ormond Street Hospital*, (3)*Institute of Child Health, UCL*, (4)*University College London*, (5)*Great Ormond Street Hospital for Children NHS Foundation Trust*, (6)*Faculty of Brain Sciences, UCL*

Background: For many children with autistic spectrum disorders (ASD) in mainstream education, the transition from primary to secondary school can be particularly stressful. To date, no previous study has developed and systematically evaluated an intervention aimed at facilitating transition at this challenging time.

Objectives: Our objective was to devise a Transition Support Pack, for families and teachers, aimed at facilitating successful transition to secondary mainstream school for a nationally representative sample of children with ASD. We aimed systematically to evaluate the effectiveness of this school-delivered, individualised, intervention in a quasi-Randomised Controlled Trial.

Methods: Participants comprised children with ASD attending mainstream primary schools (n = 42). Total 40 schools in UK. Sample mean age 11.14 years (SD:0.39); male : female ratio was 5:1. Mean FSIQ 85.92 (SD:22.27).

Recruitment comprised two phases. Schools (1 child/school) were assigned to Phase 1 control (2009/2010) or to Phase II intervention (2010/2011) samples. Children, their parents and primary/ secondary school teachers completed assessments in the last 6 months of primary school. In both phases, a follow-up was conducted

6 months after transition. Children in the control group (n= 27) received no intervention. The families and schools of children in the intervention group (n=15) received an individualised 'Transition Management Plan', based on relevant elements of the Transition Pack assessment.

Results: In the control group, teachers reported at follow-up that standardized measures of Social Difficulties increased by 0.6 SD, but in the Intervention group they had *decreased* -5.20 SD (p< 0.01). Hyperactive traits at school (FU – Baseline) were stable in controls (-0.10 SD), but reduced in those with Transitional Support (-2.73 SD, p<0.05). Emotional and Conduct problems increased in controls (0.90 SD, 0.20 SD, respectively), but had improved (-0.87 SD, -0.73 SD respectively) in intervention group. Peer problems reduced to a greater extent in the intervention group (-0.21 SD, -0.91 SD respectively). Pro-social behaviour decreased in controls (-0.74 SD), but increased in the Intervention group (0.53 SD). All results were adjusted for gender, social deprivation score, OFSTED primary and secondary ratings and IQ. No child in Phase II received additional psychiatric or other treatment as a consequence of the intervention, which was focused exclusively on enhancing support to school and family over transition.

Conclusions: The transition from primary to secondary school is stressful for most children with ASD, whether or not they have special educational support. Independent ratings by teachers indicate there is deterioration in some aspects of behavioural adjustment for most children. We devised a supportive program of indirect intervention, mediated through school and home, with preliminary evidence for positive outcomes based on independent teacher-rated measures of adjustment at 6-month follow-up.

130.147 147 ACT-Based (Acceptance and Commitment Therapy) Skills Training in Group for Adolescents and Adults with Asperger Syndrome. J. Pahnke*¹, J. Bjureberg², J. Jokinen³, T. Lundgren⁴, T. Hursti⁵, S. Bölte⁶ and T. Hirvikoski⁶, (1)*Department of Women's and Children's Health, Center for Neurodevelopmental Disorders at Karolinska Institutet*, (2)*Karolinska Hospital, Psychiatry Northwest*, (3)*Karolinska Institute, Department of Clinical Neuroscience*, (4)*Stockholm University, Department of*

Psychology, (5)Uppsala University, Department of Psychology, (6)Karolinska Institutet

Background: Although high rates of depression, anxiety and stress, as well as decreased quality of life are frequently manifested in Asperger syndrome (AS), there are few adapted evidence based treatments that address these major difficulties. Acceptance and commitment therapy (ACT) is a contextual behavioural approach that has shown to be effective for complex and chronic conditions, as well as for comorbid conditions such as anxiety and depression, although not yet evaluated in AS.

Objectives: The current research project aims at evaluating feasibility, and efficacy of an adapted ACT-based skills training group program for adolescents and adults with AS.

Methods: We evaluated the feasibility and efficacy of the 12 session ACT-based skills training group program in a school setting using a randomized controlled study design (ACT/school classes as usual). Twenty-eight students with AS (aged 13–21) were assessed using self- and teacher-ratings at pre- and post-assessment, as well as 2-month follow-up. In the skills training group, the main treatment components and processes were social skills training; values work and committed action; mindfulness and acceptance practice; functional analysis; home work; and AS-related psychoeducation. In a second phase of the project, we are now performing a pilot study of the same ACT-program for adults with AS (n=10; age range 25-65 years) in an outpatient psychiatric context. Feasibility, treatment satisfaction and efficacy will be evaluated in an open trial study design.

Results: In the first study, all participants completed the skills training and treatment satisfaction was high. Levels of stress, hyperactivity, and emotional distress in the group were significantly reduced. The group also reported increased pro-social behaviour. These changes were stable or further improved at the 2-month follow-up. In the pilot study in an adult outpatient psychiatric context, the preliminary analyses showed promising feasibility and treatment satisfaction. Furthermore, participants showed significantly reduced stress and emotional distress, as well as increased quality of life.

Conclusions: The results indicate that ACT constitutes a feasible and effective approach for facilitating everyday life and alleviating symptoms of stress and psychological distress, and increase quality of life, in adolescents and adults with AS. Several larger studies are needed to fully evaluate the ACT-program in AS. We are currently conducting a randomized controlled trial to evaluate the potential benefits of ACT-based skills training in group on stress, quality of life and autistic core symptoms in adults with AS in a psychiatric outpatient context.

130.148 148 Can the Pegasus Psychoeducation Programme Improve the Understanding, Well-Being and Functioning of Young People with an Autism Spectrum Disorder and That of Their Families? A Randomized Controlled Trial. R. K. Gordon^{*1}, L. Roughan², V. Livermore-Hardy², O. Baykaner³, D. H. Skuse⁴, M. Murin⁵ and W. Mandy⁶, (1)*Great Ormond Street Hospital and UCL Institute of Child Health*, (2)*Great Ormond Street Hospital*, (3)*Great Ormond Street Hospital for Children*, (4)*Institute of Child Health, UCL*, (5)*Great Ormond Street Hospital for Children NHS Foundation Trust*, (6)*Faculty of Brain Sciences, UCL*

Background: Despite the increased focus on early recognition and diagnosis of ASDs, very little is known about how to best help children integrate their "label" in a positive way. There is anecdotal evidence that person-centred psychoeducation and self-management training after diagnosis can enable people to develop helpful perceptions of their psychiatric condition, and can alleviate feelings of isolation and stigmatisation (Chowdhury, 2003; Proudfoot, et al, 2009). However, currently there are no evidence-based guidelines on how to communicate the diagnosis of ASD to children or their parents. Neither are there any psychoeducational packages available for this purpose.

Objectives: The study aims to evaluate the efficacy of PEGASUS, a new group psychoeducational programme designed for children with ASD and their parents. PEGASUS uses principals of self-management and cognitive behavioural therapy (CBT). The programme comprises 6 weekly sessions, each lasting 1.5 hours with separate parallel sessions for children and for parents. It aims to enable children to acquire a balanced understanding of their unique strengths and difficulties and to enhance self-management strategies tailored to the child's individual needs.

Couteur³, (1)NTW NHS Foundation Trust, (2)Institute of Health and Society, Newcastle University, (3)Newcastle University

Pilot evaluation of adapted cognitive behaviour therapy for young people with autism spectrum disorder and high anxiety.

Methods: In total, 48 children (9-14 years) with diagnoses of High Functioning Autism or Asperger's Syndrome and their parents will be recruited. Half will be randomised to attend the PEGASUS groups and half to the control group, in which they are offered no input over and above "treatment as usual". In total, five PEGASUS groups each including 4-6 children will be run. Primary outcomes are of ASD knowledge and ASD-related self-awareness assessed using a questionnaire specially developed for this study. This is measured in both children and their parents. Children also complete the Rosenberg Self-Esteem Scale, a self-concept scale and the Strengths and Difficulties Questionnaire (SDQ). Parents complete the SDQ, the Social Responsiveness Scale, the Parental Stress Index, a measure of parental self-efficacy and a measure of utility of ASD diagnosis. Data is collected at 3 time points: baseline, after 3 months (i.e. immediately post-treatment) and at 6-month follow-up, by researchers who are blind to group allocation. The Vineland Adaptive Behaviour Scale is administered at baseline and at 6-month follow-up.

Results: So far, data at baseline and Time 2 are available for 28 children and their parents (14 PEGASUS and 14 controls). Preliminary analysis suggest that parents' ASD knowledge and attitude composite scores show a significant increase following PEGASUS when children's IQ is controlled for ($F=4.89$ (df 1,25), $p=0.36$). Another promising trend is the large effect of PEGASUS on children's knowledge of their own ASD-related strengths when IQ is controlled, though this finding is not significant (partial eta squared=0.141, $p=0.053$). Partial eta squared of, 0.01, 0.06 and 0.14 are regarded as small, medium and large effect sizes, respectively.

Conclusions: This is the first study to evaluate the efficacy of a psycho-educational programme for children with ASD. The programme appears to be effective in increasing children's and parents' knowledge of ASD as well as enhancing children's positive perceptions of themselves and parents' perceptions about the diagnostic label.

Background: Many children with autism spectrum disorders (ASD) experience mental health problems (Simonoff et al., 2008), of which anxiety is common (MacNeil, Lopes, & Minnes, 2009; White, Oswald, Ollendick, & Scahill, 2009). A recent meta-analysis of 31 studies reported that around 40% of children with ASD meet criteria for an anxiety disorder (van Steensel, Bogels, & Perrin, 2011). The reasons may include their experiences (e.g. being bullied) as well as ASD characteristics (e.g. language difficulties, resistance to change, poor social skills, concrete interpretations).

Objectives: Recent studies suggest that cognitive behaviour therapy (CBT) adapted to the thinking style and needs of children with ASD can have a positive effect in reducing anxiety. The 'Exploring Feelings' program (Attwood 2004) originally developed in Australia, was modified for clinical use in the UK for young people with ASD and a co-morbid anxiety disorder. The program runs as 7 weekly sessions for 2 hours, where children and parents learn the same techniques in two separate groups. A randomised pilot study was undertaken to investigate the acceptability and feasibility parameters for use in a UK community context.

Methods: Thirty-two children, aged 9 to 13 years, were randomised to immediate or delayed therapy. Child and parent sessions were run in parallel, under the supervision of experienced clinical psychologists. The primary blinded outcome measures addressed change in overall functioning after 3 months (Clinical Global Impressions-Improvement), and in the primary anxiety diagnosis (Anxiety Disorders Interview Schedule).

130.149 149 Pilot Evaluation of Adapted Cognitive Behaviour Therapy for Young People with Autism Spectrum Disorder and High Anxiety. V. Grahame*¹, E. Honey¹, H. McConachie², J. Rodgers³, E. McLaughlin³ and A. S. Le

Results: Children met diagnostic criteria for between 1 and 6 anxiety disorders (median 3). At follow-up both parents and children in the immediate therapy group were more likely to report a reduction in anxiety symptoms, and severity of primary diagnosis reduced more, than in the delayed group.. Although all children still met criteria for an anxiety disorder, only 3 out of 17 children were referred on for further individual therapy. Fidelity of delivery of the group therapy was high, and attendance was 91%.

Conclusions: The evidence suggests adapted group-based CBT for children with ASD and high anxiety in middle childhood has the potential to be beneficial. This pilot trial has established that children and families were willing to be recruited and randomised, the format and content of the groups were feasible within UK child and adolescent mental health services, the outcome measures were appropriate for use in a future fully powered trial, the intervention was appreciated by families, and attrition was very small.

This abstract describes independent research commissioned by the National Institute for Health Research (NIHR) under the Research for Patient Benefit programme (PB-PG-0408-16069). The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health.

130.150 150 The Impact of a Social Skills Training Program On Social Competence and Social Worries in Children with an Autism Spectrum Disorder. M. Chester*¹ and A. L. Richdale², (1)*Deakin University*, (2)*Olga Tennison Autism Research Centre*

Background: Children with an Autism Spectrum Disorder (ASD) desire meaningful friendships, however, they typically lack the social competence required to navigate such social skills successfully. Social skills training programs aim to increase social competence and peer interaction and provide participants with skills for establishing and maintaining quality friendships.

Objectives: This study aimed to explore whether children with an ASD who participated in an 8-week social skills training (SST) program would display significantly greater improvements in a range of social skills and behavioural and emotional measures, compared with children who did not receive the program (control).

Methods: Forty-five children aged 8 to 12 years ($M = 10.16$, $SD = 1.26$) completed the study. All children had a clinical diagnosis of an ASD, a Social Communication Questionnaire score > 11 ($M = 18.86$, $SD = 4.95$), and IQ > 70 ($M = 85.71$, $SD = 8.66$). There were 15 children in each condition: SST with free play, SST with semi-structured play and a control group. Children were assigned to one of these three conditions based on their order of appearance on the Psychology Clinic waiting list. Within each SST condition three training programs of 5 children each were run. Data were collected pre- and post-intervention and at 3-month follow-up for all conditions. The primary outcome measures were the Social Skills Improvement System (SSIS; parent and teacher report) and the Spence Social Competence with Peers Scale (SCPS; parent, teacher, and child report). Data on friendships, loneliness, social worries, and behaviour problems were also collected. This paper focuses on outcomes for the SCPS (parent and child report) and the Spence Social Worries Scale (SWS, parent and child report) at post-intervention and 3-month follow-up.

Results: A split-plot factorial analysis of variance showed that there was a significant group by time interaction, Wilks' $L = .57$, $F(4, 82) = 6.60$, $p < .001$; Wilks' $L = .65$, $F(4, 82) = 4.91$, $p = .001$; Wilks' $L = .52$, $F(4, 82) = 7.94$, $p < .001$; and Wilks' $L = .54$, $F(4, 82) = 7.37$, $p < .001$, for parent social competence, parent social worries, child social competence, and child social worries respectively. Inspection of group means and interaction plots indicates that both SST groups generally improved over time, but the control group did not.

Conclusions: Based on our initial analyses, there were improvements in social competence and a decrease in social worries, for children with an ASD who participated in a SST program that incorporated either free play or semi-structured

play. Further analyses will be conducted, reported and discussed in our presentation.

130.151 151 Evaluation of Executive Function and Autism

Characteristics in Children with ASD Participating in Spark*. B. M. Stoesz^{*1}, J. M. Montgomery¹, E. H. MacKenzie² and K. Carpick¹, (1)*University of Manitoba*, (2)*Wired Fox Publications*

Background: Impaired executive functions (EF) and consequent weak self-regulation, or dysregulation, are found in children with attention deficit disorder, Tourette's syndrome, schizophrenia, obsessive-compulsive disorder, phenylketonuria, and Autism Spectrum Disorders (ASD) (Hill, 2004). Ozonoff et al., (2005) refer to executive dysfunction as "one of the most consistently replicated cognitive deficits in individuals with ASD" (p. 532). In general terms, development of EF predicts how well children with ASD respond to treatment (Berger et al., 2010) as well as their long-term outcomes (Szatmari et al., 1989). Deficits in the EF system are associated with impairments in communication, play, and social relationships in children with ASD (Gilotty et al., 2002). Dominick, et al. (2007) stress the importance of examining EF and self-regulation in people across the range of ASD, as well as at different age levels, within the laboratory and in day-to-day life. Recently, we showed that a self-regulation intervention program called spark*, Self-regulation Program of Awareness and Resilience in Kids (MacKenzie, 2010), improved behaviour regulation as measured by the Behavior Rating Inventory of Executive Function (BRIEF) (Gioia et al., 1996) in school-aged children with ASD (Montgomery, 2012).

Objectives: Our primary objectives were to replicate our previous finding of improvement in EF after spark* intervention in school-aged children with ASD as well as to examine the specific relationships between parent reported EF, performance-based measures of EF, and autism characteristics and behaviour before and after spark* intervention.

Methods: A group of school-aged children participating in spark* intervention groups were assessed prior to the initiation of treatment using standardized face-to-face and rating scale measures of EF [i.e., BRIEF, Gioia et al., 1996; A Developmental NEuroPSYchological Assessment (NEPSY), Korkman et al., 2007] as well as

standardized rating scales of autism characteristics and behavior [i.e., Autism Spectrum Rating System (ASRS), Goldstein & Naglieri, 2009]. spark* was administered by graduate students in school psychology who were trained in the spark* philosophy and methods and supervised by experienced clinicians. Skills addressed during the sessions included: behavioral self-regulation of hands, breathing, feet, voice, and whole body; and cognitive self-regulation, focusing and sustaining attention, determining and retaining the most important/relevant information, determining expectations, and constructing meaning. After the 10-week intervention period, the same measures of EF and autism characteristics and behaviours were re-administered.

Results: Observed and performance-based improvements in EF were found to demonstrate similar patterns as in our previous investigation of improvement after spark* intervention. Results will be discussed in terms of relationships of EF variables to autism characteristics, as measured before and after intervention.

Conclusions: The results confirm that the spark* intervention program is effective for improving the behaviour of elementary school-aged children with ASD. Parents also thought the program was a valuable program for their children and their families. Implications for programming and future research will be discussed.

130.152 152 Improving Transportability of a CBT Intervention for Anxiety in Youth with ASD: Results From a US-Canada Collaboration. J. Reaven^{*1}, A. Blakeley-Smith², T. Beattie³, A. Sullivan⁴, E. Moody⁵, S. Hepburn⁶ and I. M. Smith⁷, (1)*Univ. of Colorado Denver-JFK Partners*, (2)*Univ. of Colo. Denver-JFK Partners*, (3)*IWK Health Centre*, (4)*IWK Health Center*, (5)*University of Colorado, Denver*, (6)*University of Colorado*, (7)*Dalhousie University / IWK Health Centre*

Background: Psychiatric disorders frequently co-occur in youth with autism spectrum disorders (ASD) and markedly impede treatment progress (Levy et al., 2010). Anxiety disorders are among the most commonly co-occurring conditions (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 with encouraging results (Olatunji et al., 2010; Reaven et al., 2012; Wood et al., 2009). While it has

been critically important to develop treatments for the co-occurring anxiety symptoms in children with ASD, it is equally important to facilitate the portability and sustainability of these treatments to real-world settings (Schoenwald & Hoagwood, 2001). To bridge the gap between lab and community settings, introducing new treatments into real-world settings early in the process may inform intervention development, increase acceptability, and maximize success for clinical practice (Weisz et al., 2004). **Objectives:** 1) To train mental health clinicians outside of our research program to deliver Facing Your Fears: Group Therapy for Managing Anxiety in Children with High-Functioning ASD (FYF: Reaven et al., 2011) to fidelity; 2) to examine youth treatment outcome; and 3) to obtain acceptability data from participants to inform the intervention. **Methods:** Clinicians (e.g., psychologists/psychologists-in-training) participated in a 2½ day training plus twice monthly phone consultation. Sixteen children ages 8-14 (and their parents) participated in the study and met the following inclusion criteria: 1) current clinical diagnosis of ASD, 2) exceeding criteria for ASD on both the ADOS and the SCQ, 3) presenting with clinically significant symptoms of anxiety on the Anxiety Disorders Interview Schedule – Parent Version (ADIS-P; Silverman & Albano, 1998), and 4) verbal IQ of 80 or higher. Four 14-week group cohorts for children and their families were conducted. Multiple outcome measures were used, including the Clinical Global Impression-Improvement Scale (CGIS-I), derived from the ADIS-P, and the Screen for Child Anxiety Related Disorders (SCARED; Birmaher et al., 1999).

Results: Clinicians demonstrated significant improvements on CBT Knowledge Tests after attending training, $t(9)=2.41, p=.02$. Treatment fidelity ranged from 87-95% ($M=92%$) across all four cohorts. Significant decreases in parent-reported youth anxiety symptoms (SCARED) occurred following treatment, $t(13)=4.16, p=.001$. Further, 54% of the sample demonstrated a clinically meaningful improvement for the primary anxiety diagnosis post-intervention. Child, parent, and clinician participants completed session-by-session acceptability ratings for all four groups. FYF was viewed favorably across all participant groups ($M=4.15, SD=.50$; Likert ratings 1-5), although participants in the second group cohort yielded acceptability ratings that were significantly lower than the other three groups. Critiques from

participants were incorporated into revisions of the FYF program. **Conclusions:** Preliminary findings indicate that FYF may be successfully implemented by clinicians naïve to FYF. Clinicians achieved excellent treatment fidelity and child participants demonstrated significant reductions in anxiety symptoms post-intervention. Furthermore, results indicated that FYF was acceptable to all participants. This study supports the initial effectiveness and potential transportability of FYF for treating the anxiety of children with ASD in real-world clinical settings. Limitations include small sample size and lack of a control group.

130.153 153 Efficacy of Social Skills Group Treatments for School-Aged Children with ASDs: Short-Term Behavioral Outcomes of A Randomized, Comparative Study. L. Soorya^{*1}, A. T. Wang², D. B. Halpern², S. Soffes², M. Gorenstein², K. B. Rajan¹ and J. D. Buxbaum², (1)*Rush University Medical Center*, (2)*Mount Sinai School of Medicine*

Background: Social skills groups are commonly used treatments for children with ASDs. However, data on the efficacy of social skills groups for children with ASDs is limited by several gaps in the literature. Gaps cited in recent reviews include the need for RCTs utilizing active treatment controls, as well data on maintenance and generalization of treatment effects.

Objectives: The purpose of this study was to evaluate short-term and maintenance effects of two models of intervention: cognitive behavioral therapy (CBT) and child-directed play. The trial evaluated both neural (e.g. fMRI) and behavioral outcomes at endpoint and 3-month follow-up, although only behavioral outcome results from endpoint (i.e. 12 weeks) are presented here.

Specific hypotheses: The primary hypothesis for the study was that CBT approaches take advantage of top-down, explicit processing skills in ASD, and as such, would lead to improved performance on measures of social cognition, specifically emotion recognition, compared to child-directed play.

Methods: Participants (n=69), ages 8-11 (mean=9.88, sd =1.25) were randomized into one of two treatments: CBT or child-directed play. Both treatments involved 12, 90-minute sessions, with concurrent parent and child intervention groups. Participants were fully characterized utilizing research standard

diagnostic evaluation methods. Outcomes were conducted at baseline, week 12, and 3 months post-treatment. Outcomes included blinded assessments of emotion recognition (DANVA2, Eyes Test) and social initiation during an analogue playgroup; caregiver reports of social, adaptive, and problem behavior (e.g. Vineland, BASC2); and fMRI tasks (see related submission, 14296) . Linear mixed models were used to evaluate treatment effects on the primary outcome of emotion recognition. Repeated measures ANOVAs conducted to evaluate treatment effects on secondary outcomes.

Results: Analysis of outcomes immediately following treatment indicated improvements in both groups on several treatment outcome variables. The primary hypothesis proposing an advantage for CBT in improving emotion recognition skills was not supported (DANVA2 total correct score, estimate = 0.0437, $p=.9858$). However, the CBT group did show greater improvement on accuracy of identifying low-intensity (i.e. more subtle emotional cues) items on the DANVA2 (Child Faces low intensity, estimate = 1.03, $p=.029$). In addition, evaluation of social behavior, as measured by the Children's Communication Checklist, Social Relations subscale, suggested the CBT group was rated as exhibiting more socially appropriate behavior compared to the play therapy group ($F=4.48$, $df=52$, $p=.039$). No significant improvement in the CBT group over play group was observed for caregiver reported measures of behavior (e.g. BASC2) or adaptive behavior (e.g. Vineland).

Conclusions: This study provides data on the immediate effects of social skills group treatments in an RCT design minimizing expectancy effects of a single treatment or waitlist control designs. Overall, results from this trial suggest a modest advantage for CBT-based treatment models over play-based models for improving emotion recognition and social abilities in school-aged children with autism. Research on the durability, generalization, and potential augmentation of effects continues to be open area of investigations, particularly in light of the modest treatment effects.

Maintenance of Target Social Skills. K. C. Radley*¹, J. Hood², B. Jenson², H. Block², E. Clark² and W. M. McMahon², (1)University of Southern Mississippi, (2)University of Utah

Background: Social skills research for children with ASD has revealed that most training programs fail to produce treatment effects that generalize or are maintained beyond treatment. *Superheroes Social Skills* is a social skills training program that incorporates multiple evidence-based practices in order to overcome previously-documented social skills training shortcomings.

Objectives: The presentation aims are (1) describe multiple evidence-based practices assimilated into a single program for children with ASD; (2) review treatment, generalization, and maintenance effects of three pilot studies; and (3) describe and synthesize current research evaluating implementation of the program by trained and coached parents, as a summer camp program, and as utilized in school and clinic settings.

Methods: The program was comprised of multiple evidence-based practices: (1) video modeling; (2) peer mediated instruction; (3) self-monitoring of skill use; (4) utilization of high-interest media; and (5) training for generalization through use of homework assignments. Pilot evaluations took place in three settings: an outpatient clinical setting; a specialized school for preschool-age children with ASD; and a public elementary school. Participants included 12 children with ASD. Inclusion criteria were (1) current diagnosis of ASD; (2) score at or above ASD cutoff on multiple measure of ASD; and (3) verbal IQ at or above 69. Typical peers were also included in lessons, which were taught twice weekly for 30 minutes. Current research on the program has expanded initial pilot studies though additional evaluation in school, clinical, and summer camp settings. Additionally, parents have been trained to facilitate the program through in-vivo training and Skype-based coaching.

Treatment effects were assessed through direct observation of social engagement. Additional measures utilized in evaluation of program efficacy include the Autism Social Skills Profile, Social Responsiveness Scale, and Parenting Stress Index. The Behavior Intervention Rating Scale

was utilized to assess consumer satisfaction and social validity. Treatment sessions were filmed to aid in assessment of treatment integrity.

Results: Results of three pilot studies indicated moderate to large increases in the participants' social engagement, with effect sizes ranging from 0.74 to 1.47. Effects were observed in treatment, in generalized settings, and at maintenance. Similar effect sizes have been found in evaluations of the program in subsequent school, clinic, and summer camp-based evaluations of the program. Data indicate decreases in aggressive behaviors following social skills intervention. Evaluations on parent-facilitated social skills training indicates decreases in parent-reported stress associated with training and coaching. Treatment fidelity, social validity, and consumer satisfaction was found to be high across all studies and settings.

Conclusions: Results indicate that the multi-component training package, Superheroes Social Skills, is an effective and consumer-friendly social skills training program. Replication of intervention procedures has revealed substantial improvements in social skills as a result of program implementation. Results across studies indicate not only indicate the efficacy of the program in increasing appropriate social engagement, but document decreasing solitary play and aggressive behaviors in children with ASD and decreased parental stress.

130.155 Development of a Group Intervention Protocol for Socio-Emotional Life Skills for Adults (SELSA) with High Functioning Autism Spectrum Conditions. B. Eran^{*1}, H. Givon-Mantin¹ and O. Golan², (1)*Bait Echad Center, The Association for Children at Risk*, (2)*Bar-Ilan University*

Background:

People with High Functioning Autism Spectrum Conditions (HFASC) experience social-communication difficulties throughout their lifespan. Upon adulthood, as social and educational frameworks end and independent coping is required, many individuals with HFASC experience the social challenges they face exceed their resources. Adults with HFASC may struggle finding steady jobs and establishing social relationships. This may increase their dependence on parental support, and lead to social avoidance and to feelings of loneliness, anxiety and depression. Due to the scarcity of available

intervention protocols for adults with HFASC, this project focused on the development and evaluation of a Socio-Emotional Life Skills for Adults (SELSA) protocol. The protocol was developed under the premise that helping adults with HFASC acquire socio-emotional life skills in a peer group setting can improve their capacity to meet the social, occupational and vocational challenges of adulthood, and reduce co-morbid psychiatric symptomatology.

Objectives:

This study includes a formulation and two trial runs of the SELSA protocol for adults with HFASC. In implementing this protocol, we aimed to improve participants' emotional, communicational, and social skills in a secure peer group setting. Specific goals were increasing awareness to emotions and mental states of oneself and of others, expansion of social involvement and reduction of social isolation, while encouraging self-acceptance.

Methods:

Two groups, each of 8 adults with HFASC (an "adults" group, aged 25-40 and a "young adults" group, aged 20-30) took part in 1½ hours weekly group sessions for a period of 9 months (a total of 30 sessions). The protocol included three different sections, each of them 10 sessions long:

1. **Emotional communication**, including topics like awareness to one's own emotions, and recognizing others' emotions through non-verbal cues.
2. **Social communication**, including topics like conversation skills, use of social context, self-advocacy and conflict resolution.
3. **Social Relationships**, including topics such as creating friendships and maintaining them, dealing with complex interpersonal situations and feelings in relationship.

Each session focused on a specific topic and included a short theoretical introduction, followed by role plays, group discussions and the introduction of home assignments, which were

conducted in pairs or small groups that met independently between sessions.

Participants filled out self-report questionnaires of friendship, loneliness, anxiety and depression. Questionnaires were filled out before and after the intervention period. In addition, participants answered open-ended questions, describing their experience in the group.

Results:

Participants reported a significant increase in openness and social involvement as well as reduced loneliness. No significant results were found in anxiety and depression symptom reports. Participants' qualitative feedback highlighted improvements in self-awareness and self-acceptance, improved empathy and increased social openness.

Conclusions:

The SELSA protocol deals with core difficulties adults with HFASC experience, and allows them to learn and practice their skills in secure conditions. These preliminary results demonstrate that such structured group protocols are an appropriate way to assist adults with HFASC upgrade their coping skills with social situations, thereby encouraging their independent functioning and well-being.

130.156 156 Enhancing Face-Looking Behavior by Social Skills Training in Children with Autism Spectrum Disorders. S. Matsuda* and J. Yamamoto, *Keio University*

Background: Due to the fact that children with autism show difficulties in social interaction, researches exploring related neurological basis have been carried out. Previous studies evaluating their visual fixation patterns when observing the human face have showed that there was a correlation between the short fixation duration to the eye area and the difficulty of social interaction. On the other hand, intervention studies improving social interaction have shown that children with autism could acquire social skills, such as attention to faces and imitation of facial expressions. However, not many studies about social skills training (SST) to children with autism have evaluated its effects on the face-looking behavior.

Objectives: The purpose of this study was to examine the effect of the SST on the face-looking behavior. We also examined the relationships between the amount of change of the visual fixation and the profile of the participants.

Methods: Four boys (between 7 to 8 years old) diagnosed with autistic disorder participated in the study. Japanese standard scale of development was used to assess their developmental age. Their severity of autism was rated by CARS (Schopler, Reichler, DeVellis, & Daly, 1980). Pre - post design was applied. Before and after the SST session, the participants watched a video of a woman on a computer monitor talking to them. Their visual fixations on the video were recorded by a Tobii X120 eye tracker. Areas of Interest (AOI) for their eyes and mouth regions were created on a Tobii Studio. SST sessions were conducted 3-4 days. Training time was approximately 50 minutes per session. During the SST session, for the three target behaviors (praise, sympathy and aid), participants were trained by video-modeling and role play.

Results: Visual fixation duration for each participant for each AOI was calculated for both pre and post sessions. After the SST sessions, the fixation duration of the eye region was increased in two of the four participants. In the remaining two, the visual fixation duration of the eye region was decreased. The functional relation of the effect of SST and the profile of the participants were examined by the difference in pre- and post-visual fixation duration of the eye region. There was a significant positive correlation between the chronological age and the amount of change in the visual fixation duration of the eye region of the SST ($r = .99$, $p < .001$). With developmental age or autism severity, the amount of change had no significant correlation.

Conclusions: The results showed a tendency that the higher the chronological age, the easier to increase the visual fixation duration of the eye region by the SST.

130.157 157 The Echoes Technology-Enhanced Learning Environment: Facilitating Social Communication Skills in Children with Autism. G. Rajendran*¹, K. Porayska-Pomsta², T. J. Smith³ and O. Lemon¹, (1)*Heriot Watt University*, (2)*London Knowledge Lab*, (3)*Birkbeck, University of London*

Background: Autism Spectrum Disorder (ASD) is characterised by difficulties in social interaction. This is most pronounced in spontaneous initiations (Mundy & Newell, 2007). By exploiting their affinity for computing technology, we created the ECHOES virtual environment (e.g. Porayska-Pomsta et al., 2012) to provide experiential learning of joint attention skills for children with ASD.

Objectives: To increase the number of social initiations both within a virtual learning environment and in a real life setting. To compare differences in social initiations within the virtual environment and in a real life setting. To provide fine-grained analysis of how children perform within the virtual environment and, thereby, create a more comprehensive description of each child.

Methods: 42 children with ASD and typically developing children were exposed to a variety of environments populated by an interactive virtual character and various objects – for 10-20 minutes, several times a week, over six weeks. E.g, in a colour ball sorting task, the child interacted with the character by selecting the correctly coloured ball and 'dragging' it across the touch screen. Specifically, we targeted increases in spontaneous initiations of interactions – both towards the virtual character and human partner. Videos of children were coded for fine-grained analysis scheme based on the SCERTS framework (Rubin, Laurent, Prizant & Wetherby 2009).

Results: Data suggests differences between within and outside environment learning for the ASD group. For example, the number of social initiations (e.g. bids for joint attention) – in a real life setting – pre to post-test for both the typically developing children and the children with ASD did not change. However, there was within environment change for the group of children with ASD: who increased their number of initiations to both the virtual agent ('Andy') and human facilitator within ECHOES. Eight children increased their number of initiations to Andy, 7 produced the same number and only 4 decreased. This suggests that the heterogeneity in our ASD children may make it difficult to identify a significant group increase in initiations. However, for a number of children Andy appears to be eliciting a large increase in their spontaneous

initiations of social interaction. This is strikingly obvious when examining videos: e.g., one child who showed no initial interest in Andy spontaneously waved and said "Hi Andy!" when the agent walked on the screen in a later session. Such behaviours were extremely surprising to teachers and support workers within the school who believed the child in question to be non-communicative.

Conclusions: The 'simplicity' of the ECHOES virtual environment may have helped some children with ASD interact better with other people and virtual characters whilst they were in the environment. Further, ECHOES provided detailed information about each child beyond the standardised tests used (e.g. verbal mental age). These early results are encouraging us to 1) think of how these technologies can be used to help integrate people with ASD into society 2) how this fine-grained analysis provides a more detailed picture of the child and their potential beyond standardised measures.

130.158 158 Playing with a Robot: Enhancing Social Communication and Interaction. A. S. Roberts¹ and S. M. Shore^{*2}, (1)*Boston Higashi School*, (2)*Adelphi University*

Background:

Intelligent robots were first developed in the 1950's. Initially the focus was on cognition and problem-solving abilities. The use of robots with social-emotional intelligence, either socially evocative or socially competent, only developed more recently. These potential uses are just beginning to be explored. Some initial studies using such robots to teach play skills to autistic preschoolers found they successfully mediated turn-taking, joint attention, imitation, and proactive behavior (Dautenhahn, 2007). Recent reports of "humanoid" robots (KASPAR and Bandit) suggest they are successful in generating social attention and social smiles from more isolated severely autistic children (Dautenhahn, Nehaniv, Walters, Robins, Kose-Bagci, Mirza and Blow, 2009; Woolston, 10-17-11). Furthermore, initial results using the "humanoid" robot NAO indicate future potential for using this technology during traditional therapy sessions (Shamsuddin, 2012). PARO, a baby harp seal robot, has been used in nursing homes and hospitals to promote positive social interaction from withdrawn and

socially isolated individuals (Wada and Shibata, 2007).

Objectives:

To determine if interaction with PARO will be effective for children with autism in...

- stimulating individual/social play, language and emotional expression, attention and joint attention, and appropriate sensory play while decreasing stereotypical behavior.
- aiding students demonstrating an initial fear of PARO (with a history of fear of dogs/small animals), in decreasing that fear through repeated exposure as measured by the behavioral variables of the study.

Methods:

18 students at the Boston Higashi School (15 boys and 3 girls) with diagnoses on the autism spectrum, aged 8 to 14, participated. 8 of these students (44%) were day students while 10 (56%) were residential students, participating 24/7 based on severity of need. The students, divided into groups of 4 or 5, met once a week to "play with PARO". Over 9 sessions, each group began with 3 Free Interaction for the initial "A", then 3 each for the Facilitated Interaction and Representational Play for the "B" or intervention, and then 1 Free Interaction session for the second "A" generalization session. A repeated measures analysis of variance, other relevant statistical tools, and qualitative data was analyzed to determine if there was a significant difference in how students interacted with PARO before and after the intervention.

Results:

Preliminary findings suggest...

- Providing structure ("B") aides students in developing emotional interactions with PARO.
- Social interaction and communications increased during the intervention phase

and sensory seeking decreased as hypothesized.

- Most variables returned to pre intervention levels when structure was removed except for seeking peers out which remained improved.
- Self stimulatory behavior increased during the intervention stages, contrary to expectations, but fell below baseline levels during the generalization session.
- Fearful students decreased their levels of fear and anxiety over the repeated trials, measured by their proximity to PARO, willingness to engage in contact and observable facial expressions.

Conclusions:

It appears there are significant differences among various variables including social interaction and self-stimulatory behaviors during the intervention stage. Further research is indicated to increase the generalization effect of the intervention for students at the severe end of the spectrum.

130.159 159 Computer-Based Face Training in Autism: A Comparison of Two Programs. A. N. Sung*¹ and V. Smith², (1)University of Victoria, (2)University of Alberta

Background: Facial processing is integral to developing interpersonal relationships and successful functioning within a social group (Shultz, 2005). Individuals with autism spectrum disorder (ASD), however, experience profound difficulties in both facial recognition and expression understanding. Over the past decade, computer-based training in autism has attempted to improve face skills and social cognition. Informed by Theory of Mind, *The Transporters* (Golan et al., 2010) is an animated series designed to enhance emotion comprehension. Informed by Weak Central Coherence theory, *Let's Face It!* (Tanaka et al., 2010) includes seven interactive games designed to improve recognition of faces and facial expressions.

Objectives: To test these explanatory models by directly comparing the effects of two computer-based face processing interventions for children with ASD: *The Transporters* (Golan et al., 2010) and *Let's Face It!* (Tanaka et al., 2010).

Methods: Children aged 4 to 8 years (N = 21) were randomized to one of three conditions: *The Transporters*, *Let's Face It!* and a *no treatment control*. Before-and-after 20 hours of intervention, children were assessed in ability to: (a) comprehend facial expressions by way of non-verbal intelligence, (b) interpret facial expressions by mediating through social context, (c) label emotions in faces, (d) recognize emotion constancy and (e) recognize featural and holistic configuration of faces.

Results: Compared to children randomized to a no treatment control group (n = 7), children receiving *The Transporters* training (n = 8) or *Let's Face It!* program (n = 6) experienced no greater significant improvement. Verbal ability and age of participants were linked to performance on the facial understanding measures.

Conclusions: While findings in this exploratory study are limited due to small sample size, insignificant intervention effects suggest limitations in the social validity of *The Transporters* and *Let's Face It!* interventions. Anecdotally, parents of children receiving *The Transporters* and *Let's Face It!* interventions were overall very pleased with the experience. Almost all parents reported their children to have improved in face viewing behaviour and understanding.

130.160 160 A Computerized Interactive Game for Remediation of Prosody in Children with Autism. J. van Santen*, B. H. Langhorst, A. P. Hill, C. Conway, R. Sanger-Hahn, G. Keepers, M. Parmer, R. Ludovise, E. T. Prud'hommeaux and G. Kiss, *Oregon Health & Science University*

Background: People communicate both by what they say (utterance content) and how they say it (prosody). Prosody refers to the rhythm, loudness, timing, stress, and melody of speech. Prosody allows people to emphasize what is important to them. Prosody conveys feelings, intentions, attitudes (e.g. sincerity, contempt); the role someone has for the speaker (e.g., one speaks differently to a son vs. a policeman). Prosody conveys a host of meanings that go beyond utterance content. There is evidence that individuals with autism spectrum disorders (ASD) have prosodic deficits. They may have impaired expressive prosody (e.g., speak in a flat, or sing-song voice) and/or impaired receptive prosody

(e.g., unable to grasp feelings conveyed by others through prosody). Such prosodic difficulties may severely affect social communication in ASD.

Objectives: Creation and evaluation of a computer-assisted system for remediation of expressive and receptive prosody in children with ASD.

Methods: (1) *Participants.* Five children with High Functioning ASD, ages 6-10, participated. (2) *System.* A computer program was developed that displays -- and allows control by a therapist of -- interactive "drama books" containing videotaped scenarios, each consisting of a series of interrelated scenes enacted by child and adult actors. An identified, on-screen targeted child is shown in each scenario for whom the ASD child will speak. Each drama opens with one scene, and the next scene -- out of a possible three or four alternatives -- occurs based on a spoken response by the ASD child to the other on-screen characters. Importantly, it is both what and how something is said that drives the selection of events, highlighting prosody's role in affecting others and changing the course of events. In total, 23 drama books were developed. (3) *Protocol.* Each child participated in five half-hour remedial sessions, administered by an experienced therapist. Each session involved six drama books. The order of the drama books was randomized between children.

Results: (1) The correlation between session number and appropriateness rating (averaged over subjects) was 0.41 ($t(29)=2.369$, $p<0.0125$, one-tailed). A linear model that took into account the effects of differences in difficulty between drama books also yielded a significant result ($t(164)=1.847$, $p<0.035$, one-tailed). A permutation test for the same hypothesis (where we permuted the session numbers randomly 10,000 times) yielded $p=0.0337$, one-tailed. (2) All children thoroughly enjoyed the process. Their behavior also strongly suggested that they experienced the filmed scenarios as having a high level of realism.

Conclusions: (1) The study showed the feasibility of building a system of this type (including a substantial amount of content development that required coordination of a large movie "crew"), and of creating a remediation protocol that

children enjoy and that does not put undue strains on the therapist (key here was that the user interface for the therapist was extremely simple). (2) The children improved during the sessions. While it remains to be seen whether this improvement generalizes to behaviors in natural contexts, this is certainly a promising result given that only five sessions were given spaced one week apart.

130.161 161 Using Social Robots to Improve Directed Eye Gaze of Children with Autism Spectrum Disorders. H. Feng¹, M. Kastner², A. Gutierrez^{*3}, S. Hepburn⁴, J. Zhang¹ and M. H. Mahoor⁵, (1)*University of Denver*, (2)*Univesrity of Denver*, (3)*Florida International University*, (4)*University of Colorado*, (5)*University of Denver*

Background: Children with Autism Spectrum Disorders (ASD) experience deficits in appropriate verbal and nonverbal communication skills including motor control, emotional facial expressions, and coordinated eye gaze. Recent research suggests that children with ASD exhibit positive social behaviors when interacting with robots compared to their peers that do not interact with robots [1-3]. These positive behaviors include directing emotional facial expressions (e.g., smiling towards social partner), imitating gestures and coordinating eye gaze with other forms of communication. These investigations suggest that interaction with robots may be a promising approach for rehabilitation of children with ASD.

Objectives: The relatively emerging field of robot-assisted therapy for autism aims to utilize robotic systems to develop novel interventions for improving the quality of life for children with ASD and their families. The main objective of our research study is to investigate whether a humanoid robot can successfully be used to improve directed eye gaze skill in children with high functioning autism (HFA) or Asperger syndrome. The current project is a preliminary evaluation of how individuals with HFA interact with a humanoid robot.

Methods: Participants in this study are 8 male children ages 7-17 (M=11.5 years) diagnosed with ASD or AS. The study uses NAO, an autonomous, programmable humanoid robot from Aldebaran Robotics. Participants interacted with NAO during a series of conversations and interactive games (i.e., guessing games) across 3 sessions. During

the conversations and games, NAO asked participants questions, asked them to comply with simple requests, and provided feedback during the conversations and games. Sessions were video-recorded using cameras installed in the session room as well as through NAO's front-facing camera. Videos were later scored to obtain measures of the duration and frequency of gazes directed to the robot.

Results: Participants spent, on average, approximately 50% of the session directing their gaze towards NAO (M=49%, range= 31-82%). Participants also engaged in frequent gaze shifts towards and away from NAO during the session (M=39, range=27-79) indicating that they were directing their attention towards the robot and modulating their gaze during the sessions.

Conclusions: Overall, these preliminary findings support the aim of utilizing humanoid robots as possible therapeutic agents for individuals with ASD. These results show that participants were engaged with the robot and directed their attention to the robot during a large portion of the sessions. Data collection is on going and parallel measures of participants interacting with the examiner during identical interactions will allow a direct comparison of the interaction to human and humanoid interactive partners. These results will serve as an important basis to significantly advance the emerging field of robot-assisted therapy.

References:

- [1] B. Robins, et al., "Robot-Mediated Joint Attention in Children with Autism", A Case Study in Robot-Human Interaction, *Interaction Studies*, vol.5(2), pp.161-198, 2004.
- [2] B. Scassellati, "How Social Robots Will Help Us to Diagnose, Treat, and Understand Autism", *Procs. Int. Symp. on Robotics Research*, San Francisco, USA, 2005.
- [3] D. J. Ricks, M. B. Colton, "Trends and considerations in robot-assisted autism therapy", *IEEE International Conference on Robotics and Automation*, pp. 4354-4359, 2010.

130.162 162 Reducing Anxiety in Young People with ASD Using a Virtual Reality Environment. M. Maskey*¹, J. Lowry¹, H. McConachie¹, J. Rodgers¹ and J. Parr², (1)*Newcastle University*, (2)*Institute of Neuroscience, Newcastle University*

Background:

Young people with ASD are prone to anxiety; studies indicate around 50% of those with ASD meet criteria for at least one anxiety disorder (Simonoff et.al., 2008).

Graduated exposure and participant modelling are identified as evidence-based treatment for anxieties and phobias (Ollendick & King 2004). The characteristics of ASD, including difficulties with imagination, may necessitate adaptation of traditional methods to make them more accessible to young people with ASD. One such adaptation is the use of a virtual reality environment (VRE) to reproduce the anxiety-provoking situation. This removes the need to use imagination, and provides a way to gradually increase exposure to the target stimulus.

Objectives:

In this feasibility study, we are: 1. Exploring the use of VRE as a therapeutic tool for young people with ASD with situation specific anxiety. 2. Testing the feasibility and acceptability of the methodology, and investigating the most appropriate outcome measures.

Methods:

Up to 15 verbally fluent young people with ASD aged 8-14 years, who have situation specific anxiety, are being recruited. Each participant receives two home visits, followed by four 30 minute sessions in the VRE with a tailor-made scene specific to their anxiety provoking stimulus. During each session they receive coaching in relaxation techniques and coping self-statements. The VRE we are using is a state of the art technology known as the Blue Room (<http://blueroomsv.com/>).

During each session the child and parent rate the child's anxiety using a visual six point scale. Baseline and end point overall anxiety is measured using the Spence Children's Anxiety

Scale (SCAS, Child & Parent version). We are piloting the use of galvanic skin response indices, allowing physiological measurement of arousal to be correlated with scales. Within 6 weeks of participation, interviews are carried out with the child and parent(s) to examine views of acceptability of the methods, and any changes regarding anxiety in real life situations.

Results:

Three children have participated to date. For two children anxiety reduced markedly following VRE sessions, and was associated with excellent functional improvements in anxiety in the real life situations. One child made less progress, but thought that he needed more sessions.

One child (with anxiety related to shopping) had a confidence rating related to this situation of 2 at baseline (on a scale of 0-6, low to high confidence). After 4 VRE sessions this had improved to 6, with corresponding parent ratings changing from 0 at baseline to 4 at end of therapy. Parent and Child SCAS scores on the panic and agoraphobia subscales also decreased by more than one standard deviation. Data for all children who have completed the pilot phase will be available by the end of May 2013.

Conclusions:

Our small pilot study indicates that children are engaged with the VRE, and that four 20-30 minute sessions are effective for some children. The Blue Room VRE shows initial promise as a therapeutic tool for young people with ASD and situation specific anxiety.

130.163 163 Towards the Next Generation of Computer-Based Face Training in Autism Intervention. A. N. Sung* and J. W. Tanaka, *University of Victoria*

Background: Transfer of learning is critical to address in autism research. While investigation reveals foundations for improved interventions, study of transfer is usually challenging and most often muddling. This literature review introduces computer-based face training in autism as an intriguing transfer case study.

Of all the objects that humans encounter and recognize during the course of their lifetime, it is

the human face that most readily captures our attention. Indeed, facial-processing skills are so natural and automatic that it is claimed the vast majority of people qualify as "face experts". However, a growing body of evidence indicates that individuals with autism spectrum disorder (ASD) are less skilled in face-processing abilities (Gross, 2004; Klin et al., 2002; Osterling, Dawson, & Munson, 2002).

Over the past decade, software interventions have been developed to ameliorate such difficulties experienced by children with autism. Nevertheless, there remains a discrepancy across the literature to what extent learners improve from the small screen to the big world. While previous reviews have touched on the transfer challenge, no paper to date has organized the face training in autism literature around this central theme.

Objectives: To conduct a review of the literature that sheds light on confronting the existing transfer challenge in computer-based face training.

Methods: Peer-reviewed articles examining computer-based face training for individuals with ASD were found using the *PsycINFO*, *MEDLINE*, *ERIC*, *Applied Science and Technology Index (H.W. Wilson)*, and *Web of Sciencedatabases*. Additional studies were located by examining reference lists from search-retrieved papers. Articles included in this review (a) were primary intervention papers; (b) focused on individuals with autism across the spectrum; and (c) utilized computer-based face training programs as the main instructional delivery.

Results: Eleven studies were identified and examined based on inclusion criteria. Three levels of hierarchical transfer were described across the studies. Same face transfer indicated improvement over time in a specific set of face tasks following computerized training. Different face transfer recognized improvement in novel face tasks following software instruction. Finally, beyond face transfer encompassed improvement in broader social, emotional, communicative, and behavioral functioning in light of computer-based face intervention. Yet, inconsistencies in the findings continue to highlight an existing transfer challenge.

Conclusions: Moving the field forward, this review argues that more comprehensive intervention with improved technology and augmented face-to-face instruction is required. The next generation of computerized face training must successfully transfer learners from the small screen to the big world. While a paucity of such comprehensive interventions exist, rationale to develop them are compelling and many. Along the way, continued exploration of transfer will prove inspirational that today's learning will benefit tomorrow's success.

130.164 164 How Do Teacher's Behavior and Classroom Supports Relate to ASD Student's Behavior in Class, and Do These Factors Change As a Result of Unstuck and On Target?. C. Luong-Tran*¹, L. G. Anthony¹, E. Bal¹, M. Wills¹, M. A. Werner², K. C. Alexander², L. Cannon², G. L. Wallace³ and L. Kenworthy¹, (1)*Children's National Medical Center*, (2)*Ivymount School*, (3)*National Institute of Mental Health*

Background:

Children with autism spectrum disorders (ASD) present with executive function (EF) and social challenges in the classroom, which interfere with making transitions, following rules, planning, and reciprocating. *Unstuck and On Target*(UOT; Cannon et al., 2011) is a cognitive/behavioral EF intervention for children that includes guidelines for establishing a flexible and supportive classroom, such as maintaining a high ratio of praise-to-corrections, using active priming, providing ample visual supports, and modeling flexibility.

Objectives:

This study compares change in classroom climates in schools implementing UOT versus a social skills intervention (SS; Baker, 2003) and explores relationships between teacher behavior, classroom environment, and student behavior in both groups.

Methods:

The interventions took place in 14 mainstream elementary schools. All children had IQ>70 ($M=108.45$, $SD=18.01$), met criteria for ASD on ADOS or ADI and clinician impression, and were in the 3rd-5th grade (M age=9.52, $SD=1.02$). Ten schools (47 participants) received UOT, and 4 schools (20 participants) received SS. Groups

were initially evenly-matched for age, sex, school type, parent education level, IQ, race/ethnicity, and percent on psychotropic medication.

Teacher and student behavior, as well as classroom climate, was measured during 10-20 minute sessions at 2-3 time points during the school year. Observers blind to intervention condition rated student behaviors (negativity/overload, transitioning, social reciprocity, rule abidance, participation), teacher behaviors (use of praise, use of priming, modeling of flexibility), and classroom environment (use of visual schedule, visual of classroom rules, use of reward system) during transitions and classroom activities (e.g., lectures, seat work, group work, free-time). Classroom climate was calculated using mean teacher and classroom ratings to generate an overall rating ranging from 0 (indicating poorer climate) - 6 (more positive climate) for each school.

Paired-samples t-tests were used to measure classroom climate change between initial observations and final observations. Spearman's rho correlations were used to identify relationships between teacher behaviors, classroom environment, and student behavior (see companion IMFAR abstract related to UOT classroom outcomes) at the final classroom observation (data from all 3 time points will be presented at the conference).

Results:

There was a significant, positive increase in classroom climate ratings during the school year for schools in the UOT intervention ($t=-3.980$, $p<0.01$), but not for schools in the SS intervention ($t=-0.260$). Teacher behaviors (praise, flexibility, and priming) and classroom environment (visual of schedule, visual of rules, use of reward system) were both significantly, positively associated with student flexibility, planning skills, social reciprocity, rule abidance, transitions, and participation (ρ s:0.275-0.535, $ps<0.05$).

Conclusions:

Generalization strategies of UOT include training teachers, providing standard vocabulary to use

and coaching in the use of visual supports, praise and priming. The data indicate that the generalization strategies in UOT may result to improvements in classroom climate. In addition, children with ASD benefit from visual supports in the classroom and teacher use of praise, priming, and modeling of flexibility is related to positive student performance. Classroom supports and teacher training in basic best practices for ASD may be an important mediator of the effectiveness of UOT, and perhaps any intervention.

130.165 165 Special Education Teachers' Views about Social Skills Instruction of Elementary Children in the Autistic Spectrum. C. Papoutsis*¹ and S. Mavropoulou², (1)*University of Thessaly*, (2)*Department of Special Education, University of Thessaly*

Background: Research on teachers' views and practices about social skills instruction for persons with autism spectrum disorders (ASD) remains surprisingly scarce (Uysal & Ergenekon, 2010). However, further examination is needed given the fact that teaching social skills and social understanding remains one of the major life challenges and key curriculum areas for the education of students with ASD.

Objectives: The aim of this study was to explore special education teachers' views on several aspects of social skill instruction for their students with ASD, such as instructional priorities, teaching methods and contexts, frequency of sessions, type of activities, teaching materials as well as perceived teaching efficacy in this area.

Methods:

Participants: Ninety five (n=95) special education teachers (Mage=34.03 yrs) from public special schools in 18 different cities in Greece volunteered to participate in this study. Their average teaching experience with students with ASD was 36.51 months.

Measures. Given the lack of an appropriate measure for the above research objective, an extensive questionnaire (with a 6 or 7-point Likert-type response scale) was developed and piloted for the purposes of this study.

Results: The quantitative analysis of special education teachers' responses revealed several interesting findings. Educators assigned top

priority to the instruction of social skills as compared to teaching academic skills. Interestingly, teachers stated that their decision making for social skills instruction was heavily based on students' individual characteristics and their own evaluations rather than parental expectations and evaluations from colleagues. In addition, teachers indicated that social skills instruction was associated with the amount of available instructional time rather than specially assigned time in the daily program, and was more often based on behavioral practices, teacher-centered approaches and visual supports as compared to experiential practices. Also teachers appeared to teach social skills more often in the classroom/playground rather than in the community. Special education teachers seemed to be active in developing individualized tasks with three dimensional objects following specialized curricula for students with ASD. Lastly, teachers appeared to associate their perceived teaching efficacy with their continuing education and collaboration with colleagues within the same school, rather than with their support from other administrators (i.e. head of school, Special Needs Advisor) or professionals from diagnostic/evaluation teams.

Conclusions: This study aims to contribute to the better understanding of special education teachers' views for social skills instruction for students with ASD and its findings are discussed in the context of improving support to teachers in this instructional domain, so that they can better serve the needs of their students in special education.

130.166 166 The Challenges of Applying and Assessing CBT for Individuals with ASD in a Clinical Setting; A Case Study Series. S. B. Helverschou*¹, U. Bastian², K. Utgaard³ and P. C. Wandaas⁴, (1)*Oslo University Hospital*, (2)*Nordlandssykehuset*, (3)*Vestfold Hospital*, (4)*Vestre Viken Hospital Trust*

Background:

There is a marked discrepancy between access to specialised mental health services for people with Autism Spectrum Disorders (ASD) and reports of high rates of anxiety disorders in this group. Among anxiety disorders, obsessive compulsive disorder (OCD) in people with ASD represents a particular clinical and diagnostic challenge. Cognitive-behavioural techniques (CBT), used

either alone or in combination with medication, are generally recognized as among the most successful methods for treating anxiety disorders and OCD in the general population.

Objectives:

The present study addresses ways to improve access to mental health services for individuals with ASD and OCD by enhancing the competence of professionals in secondary services. The study explores the outcome of individually focused CBT for children and young adults with OCD and ASD referred to ordinary clinical services. The aims were to educate and support therapists in conducting CBT with these individuals; to explore necessary adjustments to therapeutic techniques; to determine the optimal number of intervention sessions needed, and to identify standardized assessment instruments appropriate for evaluating treatment effectiveness.

Methods:

Five patients were given CBT modified to meet their ASD over a minimum of 12 sessions. The therapists were educated in ASD, CBT generally, and were given monthly group supervision on modifying CBT for people with ASD. A standardised assessment strategy was employed before the treatment including IQ assessment, the Social Communication Questionnaire (SCQ) and Vineland Adaptive Behaviour Scales. Pre- Post treatment measures were Children's Yale- Brown Obsessive Compulsive Scale / Yale-Brown Obsessive-Compulsive Scale, The Aberrant Behaviour Checklist (ABC), and Goal Attainment Scaling (GAS).

Results:

Twelve to 20 sessions of CBT were associated with some improvement in all patients. Most patients needed more than the initially planned 12 sessions, and some adjustments in the therapeutic techniques were made for all patients. All the assessment instruments used to monitor behaviours during treatment showed decreased symptom severity and improved outcome post-treatment for all patients.

Conclusions:

With training and monthly education and supervision sessions, professionals in secondary services are able successfully to provide CBT modified to the needs of people with ASD. The study also shows that standardised assessment instruments can be used to evaluate treatment outcome in these individuals. CBT is a promising treatment option for people with ASD and OCD but they may need more sessions than other client groups. More research is indicated in this field, as is better professional training, better liaison between specialists, and development of more specialised interest and tertiary services.

130.167 167 Teachers' Implementation of ASD Evidence Based Practices in General Education Classrooms. M. I. Thomson*, *Autism Teaching Institute*

Background: Teaching students with ASD can be a complex and baffling experience. Evidence shows that teachers in general education classrooms are unsure how autism impacts individual students' learning, and how to select teaching strategies for such students. Prevalence figures indicate that most regular schools will have one or more children with an ASD. Although there is little research on the factors associated with student progress or lack of progress in general education classrooms, it is known that teacher training is inadequate (National Research Council 2003, McKee 2005).

Clinical research has identified effective practices to address social, communication and behavioral deficits for children with ASD. However, little research has been undertaken as to how to translate these findings into effective practice in general classrooms (National Professional Development Centre on ASD). Lack of understanding of the core impairments of ASD and their variable manifestation in each child create significant barriers to adoption of Evidence Based Practice (EBP) by teachers in such classrooms. Teacher 'uptake' of EBP increases with support that includes coaching, staff support such as extra class aides, and assessment analysis of individual needs.

A model of ASD certified training for general classroom teachers, focusing on theory informing practice with hands-on coaching and mentoring has been available in Victoria, Australia since 2006. This study includes graduates of this

training along with other teachers of primary school classrooms who teach students with ASD.

Objectives: This study has two connected aims: to examine what difference a teacher's knowledge of EBP for learners with ASD in the general education classroom makes to their practice; and to find how to provide teacher training which will improve practice. The study has two stages:
1. Pilot Study undertaken first, to test instruments to be used in the larger study.
2. Full implementation study.

Methods: This is a quasi- experimental ex post facto research project of matched groups design. The independent variables are the teacher's knowledge of ASD and EBP interventions, their sense of self efficacy with meeting the needs of students with ASD in their classroom, demographic information including total years of teaching experience, number of students with ASD previously taught, their level of autism and the level of care needed, and the data collection methods used to inform teaching practice. The dependent variable is the set of twenty-four focused interventions (Odom 2011) that have been operationally defined and set out in the observational protocol.

Expected Results:

- Information on the factors associated with teachers' effective implementation of EBP in general classrooms for students with ASD
- Practice tools for teachers, eg. an implementation checklist for teachers that can document use of EBP interventions for students with ASD in general classroom
- Knowledge of the aspects of training to target and prioritise for teachers of ASD students in general education classrooms
- Understanding of how to build on the pre-existing knowledge of teachers as they acquire experience of ASD.

Conclusions: The study promises to identify factors which retard or facilitate translation of EBP from clinical settings to the classroom.

130.168 168 Psychosocial Treatments for Children with Autism and Intellectual Disability Delivered by Non-Specialist Providers. B. Reichow*¹, C. Servilli², M. T. Yasamy², C. Barbui³ and S. Saxena², (1)*Yale University School of Medicine*, (2)*World Health Organization*, (3)*University of Verona*

Background: There are many evidence-based treatments for children with autism spectrum disorders. However, much of the knowledge has been gained from studies conducted through university settings in which the treatment was provided by highly specialized personnel (e.g., clinical psychologist, graduate students in psychology and medicine, psychiatrists). Much less is known about the effectiveness of treatments provided by personnel with less training (e.g., non-specialist providers).

Objectives: We sought to locate all studies examining psychosocial interventions for children who have an autism spectrum disorder and intellectual disability in which direct therapy services to the child were delivered by a non-specialist provider (e.g., teacher, aide, parent, nurse, general practitioner).

Methods: We conducted an electronic database search July 2012 of Medline, EMBASE, CINAHL, African Index Medicus [AIM], AFROLIB Database, Eurasia Health, LILACS, and Index Medicus for the Western Pacific [WPRIM], and PsycINFO using the search strategies described in the review protocol that can be located at http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42012002641. Articles were included if they met the following criteria: a) the study must have contained participants with autism spectrum disorders who, on average, had IQ < 70 and were under the age of 18-years-old; b) the study used a prospective group comparison design (e.g., randomized clinical trial, quasi-experimental multiple-group comparison); and c) the study involved a psychoeducational intervention in which the treatment delivered to the child was done by a non-specialist provider (e.g., teacher, aide, parent) or the intervention involved training parents to deliver the treatment to their child (i.e., a parent training intervention). Study, intervention, and outcome characteristics were double coded by two independent reviewers, and Cohen's d effect sizes were calculated for outcomes corresponding to five categories (developmental, daily skills, behavior, school performance, and family). We created harvest plots to display differential treatment effects across different conditions to examine which interventions were most effective in certain settings, when delivered by certain providers,

and/or for individuals with different levels of intellectual functioning.

Results: The search yielded 13,621 hits after deduplication, of which 262 full texts were examined. We located 35 studies meeting all inclusion criteria, 20 of which were randomized control trials. The behavior analytic interventions showed significant improvements in developmental and daily skill outcomes, however, many of these programs were very intensive with respect to the number of hours of treatment and resource allocation (e.g., therapist time, therapist supervision). Cognitive adaptation and rehabilitation and parent training programs showed less promise, but had positive outcomes in developmental and behavioral outcomes, respectively. Characteristics of the studies, intervention methods, outcomes, and effects will be presented in tables and harvest plot figures.

Conclusions: Collectively, the results of this review suggest that psychosocial intervention can be effective for individuals who have autism spectrum disorders and intellectual disability when treatment services are delivered by non-specialist providers. These findings are encouraging given the increasing global awareness and desire to foster better treatments for children in developing countries.

130.169 169 ABA, Teacch, and the Social and Empirical Validation of Evidence-Based Practices for Students with Autism Spectrum Disorders: Research-Supported Interventions for Schools, Homes, and Clinics. K. J. Callahan*, H. L. Hughes and P. Ma, *University of North Texas*

Background: Social validity refers to the acceptability of goals, procedures, and outcomes of programs and interventions by their key consumers; thus, it is highly correlated with whether or not strategies are used effectively in homes, schools, and clinics. Relatively little attention has been devoted to socially validating effective treatments for individuals with ASDs. As a result, it has been difficult for teachers, parents, administrators, and other service providers to identify valid intervention components. Equally important is recent work in the US by the National Autism Center (NAC) and the National Professional Development Center in ASDs (NPDC) to systematically determine interventions and treatments with demonstrated effectiveness for children and adolescents with ASDs. Research to

investigate interventions that have both social and empirical validation could have a significant positive impact on autism programming.

Objectives: The purpose of this study is to determine the relationship between socially and empirically demonstrated evidence-based practices for individuals with ASDs. More specifically, using data from studies identifying socially valid and empirically-demonstrated interventions, we will identify a list of recommended interventions, including components of ABA and TEACCH, which can be used as a starting point for parents, teachers, and other service providers in selecting and implementing research-proven practices.

Methods: In a previous study a survey was mailed to 324 parents, teachers, and administrators asking respondents to rate the importance (on a seven-point Likert-like scale) of 60 evidence-based components of autism interventions in school/clinical settings. Intervention components were rank ordered by overall mean ratings across all respondent groups, and categorized into five functional areas. The components were further reliably analyzed by subject matter experts to determine if they aligned with practices typically associated with ABA, TEACCH, neither approach, or both approaches. For the present study, the 60 intervention components were re-analyzed to determine the correlation between the socially validated treatments and their corresponding intervention components identified as "established," "emerging," or "unestablished" by the NAC, and "confirmed" as evidence-based practices by the NPDC.

Results: Teachers, parents, and administrators indicated consistently high levels of social validity for research-based practices in autism (mean rating = 6.27, range 3.34-6.90). All of these primary consumer groups of autism interventions ranked the components inherent within both ABA and TEACCH higher than those associated with either model alone. A comparison of the socially validated components with those identified in the NAC and NPDC studies showed a significant correlation, with 23 of 24 (95.8%) of the interventions represented on both lists of research-supported practices. ABA components

made up the largest percentage of the socially and empirically valid treatments.

Conclusions: By providing an empirically-based, rank-ordered, list of interventions with both social and empirical research support (e.g., the top-rated interventions include social skills training, functional communication training, functional behavior analysis, task analysis, discrete trial training, and visual supports) teachers, parents, and administrators in schools and clinics can make more efficient and better-informed decisions about which interventions to implement. In addition, these groups can use these validated interventions to evaluate existing curricula and develop more effective training to improve the outcomes of their autism programming.

130.170 170 Barriers to Behavior Intervention: Improving Behavioral Support Through Pyramidal Training On Treatment Fidelity Methodologies. K. B. Marshall*, M. J. Palmieri and S. M. Egan, *The Center for Children with Special Needs*

Background: Individuals with autism spectrum disorders often present with significant challenging behavior that interferes substantially with access to educational services and quality of life for their families. Comprehensive and evidence-based assessment and intervention strategies are well understood; however, it can be difficult to ensure interventions are implemented with fidelity by educators, caregivers, and treatment providers. This is especially the case in public school settings where a scarcity of technical resources, staff training, and human resources compromise implementation. Well-crafted interventions that are not supported by appropriate implementation can fail to achieve socially meaningful outcomes for the client and, further, may result in increases in maladaptive behavior due to inconsistent use of therapeutic protocols.

Objectives: This paper will present a process for systematically addressing barriers to implementation of behavior support plans within educational settings in order to ensure maximal therapeutic effect of these plans. The data reviewed will demonstrate the positive impact of applying a pyramidal training model with school teams to establish a stable procedure for monitoring treatment fidelity on plan implementation as well as plan effectiveness.

Methods: All participants underwent functional assessment procedures and were supported by behavior support plans derived directly from assessment data. To address the presence of ongoing challenging behavior a protocol was introduced to instruct the educational team on maintaining implementation fidelity. A pyramidal training model was implemented with the educational team to establish a consistent and proactive process for observation and performance feedback. Data were collected on lead educator proficiency with implementing fidelity monitoring as well as the behavior support plan implementation fidelity of all team members. The data on implementation fidelity were reviewed for co-variation with levels of challenging behavior to assess associated therapeutic effects of this process.

Results: The implementation of the pyramidal training model resulted in significant improvements in educational teams' abilities to reliably implement behavior support plans. The lead educators were able to demonstrate proficiency with executing treatment monitoring and offering performance feedback to team members. The successful acquisition of this treatment fidelity model by the educational teams was associated with positive therapeutic effects of the behavior support plans for the students. For example, in one setting the initial levels of implementation fidelity fell at 68% and following the application of the fidelity monitoring protocol fidelity was measured at 92%. Levels of challenging behavior decreased substantially to near zero as implementation fidelity rose.

Conclusions: School staff should be trained to utilize treatment fidelity monitoring as an essential component of effective behavior support plan implementation. Without appropriate fidelity monitoring procedures, clients may fail to experience the therapeutic effect of appropriately developed behavior support plans. Further, fidelity monitoring procedures provide important information for evaluating plan effectiveness as without these an intervention may be judged as ineffective when, in fact, it would result in substantial behavior change if implemented correctly. Educational teams must possess not only the ability to assess and develop interventions, but additionally to train all team

members on protocol use and monitor maintenance of correct implementation.

130.171 171 The Effectiveness of a Research-Based Parent Mediated Intervention for Youth with ASD Served in Community Service Settings. N. Stadnick*¹, L. Brookman-Frazee² and A. Stahmer³, (1)*San Diego State University/University of California, San Diego Joint Doctoral Program in Clinical Psychology*, (2)*University of California, San Diego*, (3)*Rady Children's Hospital, San Diego*

Background: Children with ASD are increasingly receiving community-based treatment services. Several treatment methods, many that include parent education, have demonstrated efficacy in controlled research settings, and improvement in child/parent functioning. Despite these efficacy data, little is known about the effectiveness of such methods in community settings. Findings from the few studies conducted in community settings suggest feasibility of implementing research-based parent education treatment in these settings, and that outcomes may be similar to those in research settings. However, limitations of this research include lack of a control group, limited attention to parent factors that may impact child outcomes, and no follow-up assessments to measure maintenance of gains.

Objectives: This study examines the effectiveness of a 12-week research-based, parent-mediated naturalistic behavioral/developmental intervention targeting social communication skills delivered in a community setting to children with ASD. This study compares child outcomes for those in the intervention and community comparison conditions from baseline to 12 weeks (immediately post-intervention) and 24 weeks (follow-up).

Methods: Participants include children ages 18 months-8 years with an "at risk" or diagnosed ASD and their primary caregiver. Children in the intervention condition receive the 12-week Teaching Social Communication (TSC) intervention (Ingersoll & Dvortcsak, 2009) delivered as part of routine care in a community setting. Families in the community comparison condition are receiving routine community-based services, excluding TSC or similar interventions. Children in the intervention condition are an average age of 46.69 months (SD = 25.72), 81% boys, and 31% Caucasian while children in the comparison condition are an average age of 65.92

months (SD = 18.45), 92% boys, and 36% Caucasian. Child outcomes are measured on the VABS-II Communication and Socialization domains, parent stress is measured on the PSI-SF and parent-child interactions are measured using observational methods. Outcomes are collected at baseline and 12 and 24 week follow up.

Results: Preliminary analyses (one-way ANOVAs using change scores) using data from the first 30 families enrolled (16 intervention; 14 comparison) suggest that children in the intervention condition demonstrate greater gains from baseline to 12 weeks than children in the comparison condition. Specifically, children who received the intervention demonstrated greater improvements on the Communication domain, $F(1, 18) = 8.21, p < .05$ relative to the comparison condition. The same trend, in which the intervention condition demonstrated greater gains, approached significance on the Socialization domain, $F(1, 18) = 2.91, p = .11$. Final multi-level analyses and 24-week data will be presented as well as analyses of observed parent-child interactions and parenting stress.

Conclusions: Preliminary data suggest that the TSC intervention may be effective when delivered by community providers, and highlight the importance of community effectiveness studies. This study offers methodological strengths (e.g., service-as-usual comparison group, follow-up data) relative to existing studies examining community-delivered interventions. While preliminary, results suggest that children in the intervention condition demonstrate improvement in communication and a trend towards improvement in social skills relative to children in the comparison condition. This type of study is particularly important as the number of children with ASD served in community settings increases.

130.172 172 Influence of Adaptive Behavior Functioning of Individuals with Autism Spectrum Disorder On Parental Adherence to Treatment Recommendations. K. Tang*, A. Dammann, K. L. Ryan and J. J. Diehl, *University of Notre Dame*

Background: Parents are an integral component of treatment for individuals with autism spectrum disorder (ASD) as they provide continuity, maintenance, and generalization of learned skills. It is crucial that when parents are involved in the delivery of treatment they adhere

to prescribed recommendations to optimize treatment effectiveness. Previous research has suggested an influence of child diagnosis on parental adherence; specifically, parents of children with a diagnosis of Asperger syndrome were less likely to adhere to behavioral treatment recommendations than parents of children with other ASD diagnoses (Moore & Symons, 2009). It remains unclear, however, whether it is the actual diagnosis of the child that influences treatment adherence, or whether this difference is related to other factors, such as adaptive behavior functioning.

Objectives: This study investigated the relationship between current adaptive behavior functioning and parental adherence to behavioral and medical treatment recommendations. We predicted that parents who reported higher levels of adaptive behavior functioning for their child were less likely to adhere to treatment recommendations than parents who reported lower levels. We also hypothesized that overall adaptive behavior functioning would predict parental adherence to treatment recommendations over and above diagnosis alone.

Methods: Two hundred and two primary caregivers of individuals with ASD anonymously completed online questionnaires. All participants were parents of individuals 21 years old or younger. Accuracy of diagnosis was screened using the Social Communication Questionnaire Lifetime. To measure current adaptive behavior functioning, parents completed the Adaptive Behavior Assessment System-Second Edition. Parents also completed the Parental Adherence Questionnaire, which looked at parental adherence to behavioral and medical treatment recommendations for children with ASD (modified from Moore & Symons, 2009).

Results: Overall adaptive behavior functioning was negatively correlated with parental adherence to medical treatment recommendations ($r = -.18, p < .05$). When controlling for diagnosis, overall adaptive behavior functioning accounted for a significant proportion of variance in parental adherence to medical treatment recommendations over and above the effects of diagnosis alone [$R^2 = .10, F(1, 121) = 4.31, p < .05$]. Overall adaptive behavior functioning was not correlated

with parental adherence to behavioral treatment recommendations ($r = -.08$, $p = .30$).

Conclusions: These data suggest current adaptive behavior functioning is predictive of parental adherence to medical treatment recommendations over and above diagnosis alone. That is, parents who reported higher levels of adaptive behavior functioning for their child, as generally seen in individuals with a diagnosis of Asperger syndrome, were less likely to adhere to medical treatment recommendations. Such deviations in treatment adherence may impede on treatment outcomes for the child. Future research should examine the extent to which specific domains of adaptive behavior functioning (rather than an overall measure of adaptive behavior skills) influence parental adherence to treatment recommendations.

130.173 173 Peer Engagement At School. M. Kretzmann*¹ and C. Kasari², (1)*University of California, Los Angeles*, (2)*University of California Los Angeles*

Background:

A child diagnosed with autism spectrum disorder (ASD) is likely to have difficulty socializing with peers. School lunchrooms and playgrounds are powerful, notorious settings for interactions between children. Yet, despite ripe and recurrent opportunities to boost social development (and academic engagement) of students during lunch/recess, teachers and administrators are usually taking a break themselves. Regularly, the responsibility for cultivating the lunch/recess experience is given to under-appreciated, underpaid, undertrained school staff. Not surprisingly, children with ASD often struggle to make productive social connections under these circumstances, as do their classmates. Given the increase in the number of children with ASD entering the general education population, the topic of their engagement with peers is timely.

Objectives:

We aimed to deliver a psychosocial intervention to participating children with ASD at school during lunch/recess. The naturalistic intervention was fashioned to 1) reduce solitary time and increase time spent engaged with peers, 2) activate school staff to facilitate peer engagement for all children,

and 3) demonstrate that children who receive the intervention perceive more peer engagement and rate their overall lunch/recess experience as better than those in the WL condition.

Methods:

We implemented the study using a randomized, wait-list-controlled design across two cohorts in four public elementary schools within a major metropolitan area in the Western U.S.A. Randomization at the school level produced two initial treatment (IT) groups consisting of 13 (two female) elementary school students with autism and a wait-list (WL) group of 11 (four female) children with ASD. Treatment was delivered daily at school lunch/recess for three weeks (15 sessions), then faded over the next three weeks (6 sessions) for a total of 21 sessions. Measurements employed included observational coding of peer engagement, behavior checklists and child surveys.

Results:

Our analyses revealed that, for participating children, the proportion of time spent alone or isolated from peers was significantly reduced in the IT group ($p = .012$) and time spent engaged with peers was significantly increased in the IT group ($p = .01$). School staff at the sites where initial treatment was delivered showed increased responsive ($p < .01$) and strategic behaviors ($p < .01$) around participants at lunch/recess compared to staff at the WL school. Children receiving the intervention reported talking and playing with more peers ($p < .01$) and having an overall better lunch/recess experience ($p < .01$) than those in the wait-list group.

Conclusions:

It is possible to increase the amount of observable peer engagement for children with ASD at school. Lunchroom and playground staff, despite being under-valued, will significantly change their behavior to improve outcomes for children with ASD and peers when presented with relevant information. Children appreciated our efforts and the cost-effectiveness of this approach suggests a good investment for all. Future directions might include increased articulation of the lunch/recess

experience for all children and a reassessment of the pay, training and supervision for the school staff given the responsibility of overseeing lunchtime and recess.

130.175 175 Theory of Mind, Friendship and Social Status in Children with Autism Spectrum Disorders. A. L. Toureille*, F. Pourre, J. Andanson and J. P. Raynaud, *CHU de Toulouse*

Background: In children with Autism Spectrum Disorder (ASD), the difficulties in social interactions contribute greatly to hinder the establishment of friendship. However, in our day care units, we observed these children have interpersonal experiences that can sometimes lead them to real peer relationships. Like all children, they get a lot of satisfaction and developmental benefits of these friendships. But we also notice that some of them seem more popular or more attractive than others. Data from the international literature and daily observation of children with ASD in group suggest that the level of access to the theory of mind (ToM) and the type of diagnosis are important factors. A better understanding of factors involved in the development of friendships among children with ASD may allow us to better support these relationships through our therapeutic interventions.

Objectives: To explore, in a group of children with ASD, whether there is a link between the status in the peer group and the following parameters: theory of mind and diagnosis. To propose to use these data in a therapeutic perspective: assessment and social skills training.

Methods: 28 children, aged 8 to 12 years treated in our day care unit participated in our preliminary study, for two consecutive school years. They were divided into 2 groups according to DSM-IV criteria: 14 had autistic disorder (299.00) and 14 had PDDnos (299.80)]. The status of each child in the group (popular, rejected, neglected or controversial) was determined from questionnaire developed by J.D Coie, K.A Dodge et H.Copotelli : Children named the three preferred and the three less appreciated children; educators gave their evaluation of peer relationships between children. The sociometric methods defined by J.C Perry allowed to determine a score of social preference and impact. The presence of ToM was measured by test scores at Smarties and Sally-Anne test. The data were processed using the software

STATVIEW (SAS Institute, USA), Chi 2 test and when it was required, by Fisher exact test.

Results: There is a statistically significant correlation: Between sociometric status and presence of theory of mind: 2/3 of children with "popular" status in the group acquired theory of mind and 90% of children with the "rejected" status have not acquired theory of mind; Between sociometric status and diagnostics. : 2/3 of children with PDDnos have a popular status, 80% of children with autistic disorders are rejected or neglected.

Conclusions: In our care unit, children with ASD discover and learn social skills, supported by cognitive workshops and educational interventions. Our results supplemented by data from the international literature can consider a number of avenues to support friendship among children with ASD: To enhance the work on theory of mind in social skills training groups; to use data from sociometry to assess, in ecological environment, the impact on social skills training strategies. Moreover, such an exploration, better identifying the most vulnerable children, can prevent the phenomenon of bullying.

130.176 176 A Naturalistic Social Communication Intervention for Minimally Verbal Children with Autism. L. H. Hampton*, J. D. Bryant, A. P. Kaiser, J. P. Nietfeld and A. Khachoyan, *Vanderbilt University*

Background: Acquisition of spoken language before age 5 is an important predictor of long-term academic and social outcomes for children with autism (Rutter, 1978). For children with autism who are not using verbal communication in social interactions even after early intervention, it is imperative to identify an effective treatment. Two interventions have been shown to impact early social communication during relatively short term treatments. Enhanced Milieu Teaching (EMT) has been found effective for increasing spoken communication in young children with autism (Hancock & Kaiser, 2011). The JASPER (Joint-Attention, Structured-Play, Emotion Regulation) intervention has been shown to increase not only joint attention and play, but also communication (Kasari, 2008). The current study examined the effects of a blended intervention (EMT-JASPER) targeting social attention, play and spoken language for minimally verbal children with

autism who have not been responsive to previous communication interventions.

Objectives: 1) Does the blended EMT-JASPER intervention improve social communication in minimally verbal children? 2) Will the effects of an initial EMT-JASPER intervention generalize to other adults who do not use the EMT-JASPER intervention strategies, and (3), those who do?

Methods: The participants included three boys with autism (MN age 51.6 months) each of whom was minimally verbal and had participated in more than two years of intervention. A multiple probe across participants single subject design was used to evaluate the intervention. A secondary multiple probe design was implemented across three therapists for each participant in order to examine generalization during baseline and treatment conditions with new partners. All interventionists were trained to fidelity on the EMT-JASPER intervention. Intervention occurred during 30-minute play sessions in a clinic setting. Every session was video recorded transcribed and coded for social communicative use of specific language target forms. Interobserver agreement averaged 96% (range 83-100%) for child communication.

Results: Each child demonstrated a large increase and an accelerating trend in spontaneous target use within six intervention sessions. The participants did not generalize to new therapists when they did not use intervention techniques (baseline condition); however, after 4-5 sessions of intervention, all children responded to the EMT-JASPER intervention with new therapists at levels similar to those observed with their first therapist. Spontaneous use of social communicative targets for each participant averaged 4.75 (SD=6.29), 4.92 (SD=2.50), and 3.79 (SD=5.62) during baseline, respectively. Spontaneous target use increased during intervention for each participant to 36.48 (SD=18.13), 30.96 (SD=15.17), and 13.20 (SD=7.04) respectively.

Conclusions: The EMT-JASPER intervention was effective for increasing spontaneous targets for these minimally students however, generalization was not observed until the intervention was implemented by the additional therapists. These findings suggest that at least initially, children with a history of minimal verbal communication

may need systematic support across partners in order to use newly learned social communication skills. This is consistent with the proposal that that joint attention is a state that is dyadic and unique between conversation partners (Tasker & Schmit, 2008). Future research should investigate the effectiveness of introducing multiple interventionists including familiar communication partners during blended EMT-JASPER sessions to promote faster generalization.

130.177 177 Early Predictors of Pragmatic Language Skills in School-Age Children with ASD. B. L. Williams*, *UCLA*

Background: Children with autism spectrum disorders (ASD) frequently display deficits in pragmatic language skills and social communication. These difficulties emerge when children try to engage in age-appropriate social relationships, often wanting to establish friendships, but lacking the skills to do so. As such, they report more loneliness than their neurotypical peers (Bauminger & Kasari, 2000). The difficulties they experience may be the result of underlying social communication deficits, and difficulties with the pragmatics of language. Even when children with ASD achieve optimal outcomes they continue to demonstrate pragmatic language difficulties and social awkwardness (Sutera et al., 2007). Researchers frequently conclude pragmatics skills are a component of language consistently impaired in individuals with autism (Kelley et. al, 2006). Research on early social communication skills that predict later pragmatic skills in children with ASD may inform the targets of early interventions.

Objectives: Objectives are to test if joint attention and symbolic play skills in children with ASD ages 3-4 are associated with higher conversation quality scores in children at ages 8-9.

Methods: Participants in this longitudinal study include 23 children with ASD seen at 3-4 years and later at 8-9 years. These children participated in a larger study and are included here since they were given Module 3 of the Autism Diagnostic Observation Schedule – Generic (ADOS) that involves several presses in which pragmatic language can be assessed. At age 3-4 children received a battery of evaluations to assess communicative interactions, play skills, receptive and expressive language, and cognitive

development. Specifically, one of the tests included the Structured Play Assessment (SPA).

At age 8-9 children were assessed on the ADOS, Module 3. Portions of the structured interview that did not call for materials were assessed to specifically analyze pragmatic language in conversations in unstructured contexts without visual cues.

Videos were analyzed using the Yale-Adaptation of the Pragmatic Rating Scale (Y-PRS). This scale is based on ADOS videotaped interviews and modified from the Pragmatic Rating Scale developed by Landa et al. (1992). The PRS identifies 30 pragmatic behaviors frequently reported to be adversely impacted in ASD. The scale is divided into 3 categories: (1) Pragmatic Behaviors, (2) Speech and Language Behaviors, and (3) Other Communicative Behaviors.

Results: Significant associations were found between symbolic play types and frequency on the Structured Play Assessment at age 3-4 and subsequent conversation quality scores and pragmatics ratings in conversation at ages 8-9. The associations between joint attention and pragmatic language scores were non-significant.

Conclusions: Symbolic play types represent flexibility in play skills. These skills early in development were associated with later conversational quality. Thus, the presence of flexibility in play may allow children to further develop their representational, and social conversational abilities through multiple interactions with adults and peers. The extent to which specific aspects of pragmatic language are influenced by earlier social communication skills should be further investigated.

130.178 178 Assessment and Intervention for Disorders of Reading Comprehension in Students with Autism Spectrum Disorders. K. B. Marshall^{*1}, T. M. Newman¹, J. Rohrer¹ and M. D. Powers², (1)*The Center for Children with Special Needs*, (2)*Yale University*

Background: Students with Autism Spectrum Disorders (ASD) often experience academic weaknesses, particularly with language-based skills such as reading comprehension. Although researchers have found that not all individuals with ASD have reading comprehension

weaknesses, specific language processes involved in reading comprehension are common skill deficits and impact tasks such as making inferences, identifying main idea, and drawing conclusions in text. In teaching individuals with ASD, direct instruction utilizing the principles of applied behavior analysis (ABA) has been found to be a highly successful methodology for skill development across the domains of language, socialization, and academics. However, applying these methods to reading comprehension instruction for individuals with ASD has not been well documented.

Objectives: We sought to determine whether the application of instructional strategies derived from ABA to the task of reading comprehension would foster skill mastery in learners with ASD who have been making limited progress in reading comprehension.

Methods: A reading comprehension curriculum and instructional sequence was developed based on the principles of ABA. The particular skills addressed included identification of non-fiction text features, the identification of text structures, selection and completion of graphic organizers corresponding to text structures, comprehension monitoring, and identifying main idea. This protocol was piloted with a nine-year-old student with ASD with average single word reading and reading fluency skills, but weaknesses in both literal and inferential comprehension. The curriculum was implemented four days a week for two hours over a four-week period. Direct instruction procedures were utilized across all lessons. Data were reviewed daily in order to assess progress and determine needed changes. A combination of high-preference content and grade-level curriculum content were presented across three instructors to assess generalization of skills. By April 2013 a total of 3 students will have completed the intervention.

Results: Results from the pilot study demonstrate that the student mastered targets across seven lesson plans, including distinguishing four non-fiction text structures with selection and completion of a corresponding graphic organizer for each. Monitoring for comprehension through the use of marking stop points in a text and self-questioning with open-ended questions selected from a visual at each stop point was mastered. In

addition, the student made significant progress on identifying main idea, moving from single words, to phrases, with an eventual progression to identifying main idea of a paragraph.

Conclusions: The program was successful in increasing skills across all seven lesson plans in the series for a nine-year old student with ASD. Implementation of the curriculum with additional participants has begun. The generalization of this intervention is currently being conducted in public school settings and therefore will assess the functionality of this curriculum when presented in a less-intensive teaching environment by school staff.

131 Cerebellar Contribution to Autism Spectrum Disorders

Moderator: T. Hensch *Harvard University*

Organizer: T. K. Hensch *Harvard University*

Cerebellar abnormalities in the autistic brain were first reported in the late 1980s but have remained largely unexplored from a mechanistic standpoint. This symposium links recent systems, cellular and molecular approaches which have rekindled interest. As a group, we will explore how structural and functional differences in the cerebellum contribute to the etiology and specific symptoms of autism spectrum disorder, and more importantly how these may be reversed. A functional topography has recently emerged in the human cerebellum: different regions process different types of information based on the connectivity of specific areas of the cerebellum with sensorimotor, cognitive and affective processing regions of the cerebral cortex. These findings offer a new theoretical framework within which we can examine the potential role of the cerebellum in autism. Human imaging of autistic individuals in comparison with children with cerebellar damage due to tumor removal studies will be presented. In parallel, Lurcher mutant mouse chimeras, with varying numbers of Purkinje cell loss in a time-frame that is equivalent to the last trimester in humans, have been tested for stereotypy, attention, spatial memory, and behavioral inflexibility. These will be considered in terms of the disconnection that occurs between the cerebellum and forebrain structures like the prefrontal cortex. Based upon the embryology, development, inputs, connectivity, and emerging insights into function, the cerebellum stands at the cross-roads of integration of sensory input, cognitive processing, and motor output. All three of these systems are perturbed in autism suggesting an important involvement of the cerebellum in the etiology. Yet, the pathogenesis of autism remains poorly understood, and contribution of cerebellar dysfunction to these disorders is unclear. A comprehensive time-series analysis of the genome-wide RNAs expressed every 24-hours in the mouse cerebellum from embryonic day 11 through birth and thereafter provide powerful bioinformatic tools. For instance, a gene regulation network can be built where Neuroigin, a synaptic adhesion molecule, is a key factor. Neuroigin-3 knock-out mice exhibit disrupted hetero-synaptic competition, ectopic climbing fiber synapse formation, and

perturbed metabotropic glutamate receptor- dependent synaptic plasticity (mGluR-LTD). These phenotypes could be rescued by re-expression of neuroigin-3 in juvenile mice, highlighting the possibility for reverting neuronal circuit alterations in autism after completion of development. Specific wiring defects in cerebellar circuits reveal an unexpected convergence of synaptic pathophysiology in this non-syndromic form of autism with those in Fragile X syndrome. Tuberous sclerosis complex (TSC) provides another ideal model of syndromic autism. It is caused by mutations in either of the TSC1/2 genes upstream of mammalian target of rapamycin (mTOR), whose excessive activation is believed to be pathogenic. Novel roles for Tsc1 in Purkinje cell function now define, for the first time, a molecular basis for investigating the cerebellar contribution to cognitive disorders such as autism. Importantly, treatment of mutants with mTOR inhibitor, rapamycin, starting in early development prevents both pathological and behavioral deficits. The reversibility of both syndromic and non-syndromic mouse models offers potential treatment options for core symptoms of autism, as well as novel insight into cerebellar contributions to cognition.

131.001 The Cerebellum and Autism: Imaging and Clinical Evidence. C. J. Stoodley*, *American University*

Background: Cerebellar structural and functional differences have been described in autism, but it is not clear how these differences contribute to the etiology and specific symptoms of the disorder. Recently, it has been established that a functional topography exists in the human cerebellum: different cerebellar regions process different types of information based on the connectivity of specific areas of the cerebellum with sensorimotor, cognitive and affective processing regions of the cerebral cortex. These findings offer a new theoretical framework within which we can examine the potential role of the cerebellum in autism.

Objectives: In a series of three studies, we aimed to establish the structure-behavior relationships in the cerebellum for individuals with autism as well as a comparison group of children with cerebellar damage due to tumor removal.

Methods: The first study examined the convergence of structural findings in the cerebellum from published neuroimaging studies by conducting an activation-likelihood estimate meta-analysis. The second study analyzed gray-matter differences in children with autism compared to age-matched control group with voxel based morphometry. The third study examined whether children with cerebellar damage following tumor removal show autism-like

symptoms, depending on the region of the cerebellum that was damaged. To do this, we performed voxel-based lesion-symptom mapping in a group of pediatric cerebellar patients.

Results: In the first study, the main cerebellar region found to have abnormal gray matter in ASD is associated with social and emotional processing and the default mode network in healthy and clinical populations. The results of the second two studies are pending final analyses. We predict that we will show convergence between the meta-analysis results, the prospective voxel-based morphometry findings, and the regions of the cerebellum that, when damaged, yield autism-like symptoms.

Conclusions: Cerebellar dysfunction has been described in several developmental disorders, including attention deficit disorder, developmental dyslexia, and autism, yet different cerebellar regions are implicated in each disorder. Data from autistic and cerebellar patient populations provides the opportunity to examine how these cerebellar differences contribute to the hallmark symptoms of autism in social, language, and motor domains.

131.002 Integration of Molecular, Anatomical and Functional Roles of the Cerebellum in Autism Spectrum Disorders. D. Goldowitz*, *University of British Columbia*

Background: Based upon the embryology, development, inputs, connectivity, and emerging insights into function of the cerebellum, this brain region stands at the cross-roads of integration of sensory input, cognitive processing, and motor output. That all three of these systems are perturbed in autism speaks to an important involvement of the cerebellum in the etiology of autism spectrum disorders (ASD).

Objectives: In this presentation two sets of data will be presented that converge on a system's approach to understanding potential roles of the cerebellum in autism.

Methods: We have created a comprehensive time-series analysis of the genome-wide RNAs expressed by the cerebellum in the mouse from embryonic day 11 and each 24-hour period until birth and then 72-hour intervals until postnatal day 9 (<http://www.cbgrits.org>). Using

bioinformatics tools to query these data we can construct or test hypotheses that emerge from event-based or gene-based approaches. Additionally, to explore the role of the Purkinje cell in cognitive function we have used a modification of the Lurcher mutant mouse that loses all of its Purkinje cells in a time-frame that is equivalent to the last trimester in humans. By combining Lurcher mutant and littermate wild-type 4-cell embryos to make experimental mouse chimeras, we produce a series of mice that have varying numbers of Purkinje cell loss. These mice have then been tested for stereotypy, attention, spatial memory, and behavioral inflexibility.

Results: The transcriptome work permits a molecular analysis of gene expression that might underlie ASD. From a gene-centric perspective, members of the neuroligin family have been implicated in autism. By querying the CbGRiTS database we find that Neuroligins 1 and 3 are dynamically expressed in cerebellar development and one can identify other molecules that are expressed in a similar pattern or in a manner that proceeds or precedes Nlgn gene expression. In this manner we can build a gene regulation network where Nlgn is a key molecule. We can also query from an event related perspective relative to key events in cerebellar development, such as genes related to the birth of Purkinje cells or the major period of parallel fiber synaptogenesis. The connections between the cerebellum and other brain regions are presumably altered in Purkinje cell-deficient mice. Accordingly, we find that cognitive tasks are impacted by decreased numbers of Purkinje cells.

Our behavioral studies have demonstrated a correlation between higher cognitive functions and the number of cerebellar Purkinje cells. We find significant correlations with deficits in executive function, working memory and repetitive behavior and Purkinje cell number. For example, in two different paradigms we find an increased number of perseverative errors in mice with decreased numbers of Purkinje cells.

Conclusions: This work provides insights into the molecular and functional underpinnings of autism-related phenotypes. We have begun to build gene networks that emerge from genes found in humans that are implicated in ASD and to explore how to explain our functional findings as a disconnection between the cerebellum and

forebrain structures with a focus on the prefrontal cortex.

131.003 Cerebellar Plasticity and Wiring Defects in a Rodent Model of Non-Syndromic Autism. P. Scheiffele*, *University of Basel*

Background: Human genetic studies have led to the identification of a significant number of autism risk genes, reflecting a significant genetic heterogeneity of the disorder. Monogenic syndromes, such as Fragile X, include autism as one of their multi-faceted symptoms and have revealed specific defects in synaptic plasticity. However, it remains unclear whether non-syndromic forms of autism share common neuronal alterations. In this study we performed a detailed analysis of a mouse model for a non-syndromic form of autism associated with a loss-of-function in neuroligin-3, a gene that encodes a synaptic adhesion molecule.

Objectives: We analyzed functional and structural consequences of neuroligin-3 ablation in cerebellar circuits. The potential reversibility of developmental phenotypes was tested by re-expression of neuroligin-3 in the adult nervous system.

Methods: We examined subcellular and ultrastructural consequences of neuroligin-3 ablation. The function of cerebellar circuits was further assessed using electrophysiological recordings and behavioral assays.

Results: Neuroligin-3 knock-out mice exhibited disrupted hetero-synaptic competition, ectopic climbing fiber synapse formation, and perturbed metabotropic glutamate receptor-dependent synaptic plasticity (mGluR-LTD). Disruption of mGluR-LTD is also a hallmark of Fragile X, a syndromic form of autism. These phenotypes could be rescued by re-expression of neuroligin-3 in juvenile mice.

Conclusions: We discovered an unexpected convergence of synaptic pathophysiology in a non-syndromic form of autism with those in Fragile X syndrome. Our rescue experiments highlight the possibility for reverting neuronal circuit alterations in autism after completion of development. Finally, our study highlights specific wiring defects

in cerebellar circuits caused by an autism-associated mutation.

131.004 Autism in Tuberous Sclerosis: The Case for the Cerebellum. M. Sahin*, *Boston Children's Hospital*

Background: The pathogenesis of autism remains poorly understood, and contribution of cerebellar dysfunction to these disorders is unclear. Tuberous sclerosis complex (TSC) provides an ideal model for autism research, given the very high rates of autism spectrum disorders associated with TSC and its increasingly well-characterized genetic and molecular basis. TSC is caused by mutations in either the *TSC1* or *TSC2* genes. Both genes encode for proteins that are upstream of mammalian target of rapamycin (mTOR) and mutations in *TSC1* or *TSC2* lead to upregulation of mTOR. Excessive mTOR activation is believed to be pathogenic in this disease.

Objectives: We asked whether cerebellar *TSC1/2* dysfunction contributes to the pathogenesis of ASDs. In particular, we focused on the main output neuron of the cerebellar cortex, the Purkinje cells.

Methods: To investigate the role that cerebellar *Tsc1/2* dysfunction plays in autism, we generated Purkinje cell *Tsc1* mutant mice (Tsai et al., *Nature* 2012). We examined the effects of *Tsc1* loss specifically in Purkinje cells of the cerebellum using immunohistochemistry, electrophysiology and behavioral analyses.

Results: Purkinje cell *Tsc1* mutant mice displayed pathologic features seen in autism, including Purkinje cell loss and elevated markers of neuronal stress. Mutant Purkinje cells had aberrant morphology in terms of cell size, axonal projections and dendritic spine structure and density. Furthermore, both heterozygous and homozygous loss of *Tsc1* in mouse cerebellar PCs led to autistic-like behaviors – social impairment, restrictive/repetitive behaviors, and abnormal vocalizations – in addition to excitability defects. Importantly, treatment of mutants with the mTOR inhibitor, rapamycin, starting in early development prevented both pathological and behavioral deficits.

Conclusions: These findings demonstrate novel roles for *Tsc1* in Purkinje cell function and define,

for the first time, a molecular basis for investigating the cerebellar contribution to cognitive disorders such as autism. They also provide us with a mouse model in which we can test novel hypotheses with respect to the neuronal circuitry and developmental time windows associated with autistic-like behaviors.

Services Program

132 Services

132.001 Referral to and Contact with Early Intervention Services Among Children with Developmental Concerns. M. E. Villalobos*¹, J. A. Pinto-Martin² and D. S. Mandell³, (1)*Children's Hospital of Philadelphia*, (2)*University of Pennsylvania School of Nursing*, (3)*Perelman School of Medicine at the University of Pennsylvania*

Background: It is well documented that children with developmental delays benefit from early intervention (EI) services—particularly when they are begun earlier in life. Despite the positive outcomes associated with EI and the fact that EI programs provide free developmental evaluations without requiring a diagnosis, physicians often do not refer when delay is identified or suspected.

Little is known regarding physician referral behavior and parent follow-through with recommendations in children with developmental concerns.

Objectives: The present study aimed to determine factors associated with pediatricians' referral of children with developmental concerns to early intervention services (EI) and parental contact with EI following referral.

Methods: In one pediatric practice, records for all 15- and 30-month well-child visits occurring within calendar year 2005 were reviewed (n = 869). Records were abstracted for the 230 children for whom the physician or parent expressed a developmental concern. Two logistic regression analyses were conducted; the first examined predictors of referral and the second examined predictors of parents' contacting EI after referral.

Results: Among children for whom developmental concerns were noted, 62% were referred to EI. In adjusted analyses, children of mothers with language barriers (odds ratio [OR] = 0.35, p = 0.018) and those for whom the parent, not the pediatrician, raised the concern (OR = 0.19, p =

0.002) were less likely to be referred. Of referred families, 45% contacted EI. In adjusted analyses, those cases in which the parent and pediatrician both had concerns were more likely to contact EI (OR = 3.41, p = 0.004). Neither referral nor follow up were predicted by child demographics, specific developmental concerns, or the results of developmental screening.

Conclusions: Only 62% of children for whom delay was noted were referred to EI and less than half of those were referred contacted EI. Our results suggest that language may play an important role in follow-through with treatment recommendations in young children. It also appears that parent concern alone is not likely to necessitate a referral. Further investigation of communication related factors between the parents and the pediatricians may elucidate the underlying challenges with EI referral and enrollment.

132.002 Examining Eligibility for Services Among Adolescents with ASD Transitioning Into Adulthood. L. J. Lawer*¹, D. S. Mandell², R. I. Field¹, S. C. Marcus³ and C. J. Newschaffer⁴, (1)*Drexel University*, (2)*Perelman School of Medicine at the University of Pennsylvania*, (3)*University of Pennsylvania*, (4)*A.J. Drexel Autism Institute*

Background:

Little is known about the healthcare experience of adolescents with autism spectrum disorders (ASDs) as they transition into adulthood. Research suggests that the need for services among adolescents with ASDs continues and perhaps increases during this transition. Research in other areas indicates that the transition into adulthood is critical in establishing social, developmental and healthy adult life trajectories. The delivery of healthcare during this transition has been found to be suboptimal for adolescents with other psychiatric disorders; less is known about how adolescents with ASDs fare during this transition. The social and communication deficits associated with ASDs may exacerbate challenges in navigating systems. Since almost half of children with ASDs receive services through Medicaid, this system is likely an important healthcare provider for adolescents with ASDs. It is not known whether or how they remain eligible for Medicaid-reimbursed services as they age.

Objectives:

The objective of this study was to compare the proportion of adolescents with ASD who remain eligible for Medicaid-funded services as they age into adulthood with that of adolescents with intellectual disability.

Methods:

The data source was Medicaid eligibility and encounter files from claims from all 50 states and the District of Columbia. The sample of adolescents with ASD (n=4,183) included individuals ages 16-19 who had at least two Medicaid-reimbursed claims associated with an ASD (ICD-9 code 299.XX) in the primary position in 2001. The comparison group (n=21,857) included individuals with an intellectual disability (317.XX – 319.XX) diagnosis. Individual-level characteristic variables included age, race, gender, co-occurring diagnoses, and eligibility (duration and type).

Kaplan Meier curves were generated to determine differences in loss of eligibility from 2001-2005. Ongoing analyses include regression models to assess change in the rate of disenrollment and reenrollment over time between the groups.

Results:

Over half (58.5%) of adolescents with ASDs maintained Medicaid eligibility throughout the study period compared with 62.5% of adolescents with intellectual disability. Preliminary results indicate that African American adolescents in both groups are more likely to disenroll from Medicaid as they age than adolescents of other races/ethnicities. Adolescents with an ASD who remained enrolled in Medicaid and accrued an intellectual disability diagnosis (44%) were less likely to disenroll than those who remained enrolled and did not accrue an intellectual disability diagnosis (19%).

Conclusions:

More than half of adolescents with ASDs maintained eligibility for Medicaid as they aged into adulthood; however, they fared slightly worse than adolescents with intellectual disability in maintaining eligibility. Preliminary analyses suggest that adolescents in both groups from

underserved and underrepresented communities may experience more disruption in eligibility than white adolescents. The accrual of an intellectual disability diagnosis among almost half (44%) of adolescents with ASD suggests that diagnosis switching or supplementing may be necessary to maintain eligibility. Given the expansion of Medicaid under the Affordable Care Act and the growing population of aging individuals with ASDs, the results of this study will help identify and disseminate healthcare policy that will allow for access to services for adolescents with ASD as they age into adulthood.

132.003 Service Use and Needs Among Those with an ASD in Adolescence and Young Adulthood. H. L. Hayward^{*1}, T. Cadman¹, N. Gillan², H. Eklund¹, D. M. Howley¹, J. Findon¹, H. Clarke¹, J. Zinkstok³, G. M. McAlonan¹, J. Beecham⁴, K. Xenitidis⁵, E. Simonoff¹, D. G. Murphy⁶, P. Asherson¹ and K. F. Glaser⁷, (1)*Institute of Psychiatry, King's College London*, (2)*King's College London, Institute of Psychiatry*, (3)*Bethlem Royal Hospital*, (4)*London School of Economics and Political Science*, (5)*Maudsley Hospital*, (6)*Institute of Psychiatry, King's College London*, (7)*King's College London*

Background: While many studies have investigated service use and needs of children with developmental disorders (e.g. ASD) to date little is known about this issue for these groups as they reach adolescence and young adulthood.

Also, the lack of adult services for those with ongoing needs and functional impairments (in particular among those with high functioning autism, HFA) mean that family members become integral to the care of these clinical groups.

Hence, research into the needs of young adults with an ASD (and their carers) is important in order to design and implement appropriate and effective care programmes.

Objectives: To investigate needs and other correlates of service use (e.g. medical and demographic) among those diagnosed with ASD in adolescence and young adulthood.

Methods: An observational study with young people aged 14 to 24 with an ASD (diagnosed using the ADI-R) (n=87) and with their parents or partners (usually mothers) (n=101). Face-to-face interviews and questionnaires were used to assess needs, as well as demographic and health factors associated with service use (e.g. psychiatric symptoms and medication use) at adolescence and young adulthood.

Results: All young people met diagnostic threshold for an ASD; yet 44% were not receiving any kind of services. Among our generally HFA sample there was a high level of psychiatric comorbidity but few were formally diagnosed or were seeing psychiatric services. For example, close to half of our sample met DAWBA criteria for attention deficit hyperactivity disorder (ADHD) but only 1 in 3 reported the diagnosis. Parents reported an average of 10 total needs with the most frequently reported needs concerning exploitation risk (reported by 83% of participants), ability to get and prepare enough food (73%), money budgeting (72%), looking after the home (63%) and social relationships (63%). Moreover, all reported needs were largely met by families rather than services. In the multivariate analysis, meeting DAWBA criteria for a comorbid psychiatric condition (e.g. ADHD, GAD) was the only predictor of service use even when other factors such as age and socio-economic status were taken into account. However, parental education and young person's autism symptoms were significantly associated with medication use.

Conclusions: Despite a high prevalence of psychiatric comorbidities and needs 44 % of this HFA sample was not being helped by services. The only significant correlate of service use among this clinical group was the presence of a psychiatric comorbid condition (even when core ASD symptoms and other medical and demographic factors were taken into account). In addition, 18% of our sample reported using either ADHD or Anti-Depressant medication providing evidence for the pharmacological treatment of the comorbid difficulties rather than the core symptoms of ASD. Our findings suggest that lifetime autism-specific services are required to meet the complex needs of people with ASD.

132.004 Feasibility and Reliability of an ASD Systematic Screening Program in France. S. Baduel*, Q. Guillon and B. Roge, *University of Toulouse*

Background: The American Academy of Pediatrics recommends that each child should be screened for an ASD risk from 18 months of age. In France, the *Haute Autorité de Santé*(2005) gives the same recommendation. Therefore some practical considerations like professional training, validation of screening tools, and creating coordinated professional networks must be

considered in order to reach this goal. However lack of sufficient materials in these domains lead us to conduct the present research.

Objectives: To determine the feasibility and the reliability of implementing an ASD systematic screening program for 24 months old children in *Midi-Pyrénées*(south-west region of France).

Methods: Child primary care professionals (pediatricians and child care workers) were first trained to detect signs of ASD in young children. In a second step, these professionals were asked to propose every parent to be enrolled in the program. Parents filled out the M-CHAT (Modified-Checklist for Autism in Toddlers) and professionals administrated the five observation items of the CHAT (Checklist for Autism in Toddlers) at 24 months of age. The five observation items of the CHAT were administrated at 30 and 36 months of age. Children who failed at least one key item at 24 months were evaluated with the ADOS module 1, the PEP-R, the Griffiths Mental Development Scales and the VABS. A follow-up assessment was conducted at 36 month-olds to establish the final diagnosis.

Results: Child primary care professionals screened 1160 children at 24 months; 33 children failed the screening and were clinically and developmentally evaluated with the above-mentioned tests. Among them, 16 received a final diagnosis of ASD. Sensibility, specificity, positive predictive value, negative predicative value was calculated for the M-CHAT (56%; 99%; 47%; 99%), the CHAT (93%; 99%; 65%; 99%) and combination of both tools (93%; 98%; 51%; 99%).

Conclusions: This screening program increased child primary care professionals' awareness of early signs of ASD. The CHAT and the M-CHAT appeared to be effective as to the screening of developmental disorders, such as ASD. Moreover, children screened at risk for ASD benefited from early diagnosis and early intervention. Overall, this study enabled us to create a network of screening, diagnosis and intervention professionals.

132.005 Connections for Students with ASD: The Transition From Intensive Behavioural Intervention to School. B. Robertson*¹,

J. Williams², S. Hardy¹ and A. Toritsyn³, (1)Ministry of Children and Youth Services, (2)Ministry of Education (Ontario, Canada), (3)Ministry of Education, Government of Ontario

Background:

In Ontario, Canada, Intensive Behavioural Intervention (IBI) is an intensive application of applied behaviour analysis (ABA) delivered through the Autism Intervention Program funded by the Ministry of Children and Youth Services. IBI uses the principles of ABA, in a one-on-one setting, to teach new skills in an intensive format (20-40 hours per week). ABA is provided in all of Ontario's publicly-funded schools to students with autism spectrum disorders (ASD) and is supported through Ministry of Education policy requirements on the use of ABA instructional practices, where appropriate, and in accordance with students' individual education plans.

The *Connections for Students* model was developed by the Ministries of Children and Youth Services and Education to support school-aged children transitioning from IBI therapy services to ABA instructional methods in schools. Through the model, each child is supported by a multidisciplinary transition team that includes the parent(s), teacher, principal, an ASD consultant and other professionals as required. Teams are established approximately six months prior to the child leaving the Autism Intervention Program and continue to support the child for at least six months after entry into or continuing ABA instructional methods in school.

Objectives:

To determine the effectiveness of the *Connections for Students* model in supporting school-aged children transitioning from IBI therapy services to ABA instructional methods in publicly-funded schools.

Methods:

The model was piloted in 2009-10 in 16 school boards. 477 children transitioned through the *Connections for Students* model. A mixed-method approach of quantitative and qualitative data collection and analysis was utilized including:

- Model Compliance Checklists;
- Surveys of parents and transition team members;
- Reports from local school board and community service provider partnerships; and,
- Assessments of student outcomes, including percentage of children who met individual expectations for demonstrating generalization/transfer of skills and knowledge; following classroom routines; demonstrating school-appropriate behaviour; and daily attendance.

Results:

Parents were predominately satisfied with the model implementation. 80% were satisfied with the manner in which transition teams worked with their child, and 73% agreed that transition teams benefited their child after discharge from the AIP. Transition teams' level of collaboration in the areas of respecting team expertise, promoting open communication, and supporting parent engagement were regarded as exceptionally high. Students who participated in the model achieved positive results in meeting the expectations for school attendance, skill transfer/generalization and following school routines. Data regarding student performance in the AIP was shared with school boards in advance, improving programming for children transitioning to school.

Conclusions:

The *Connections for Students* model was effective in supporting school-aged children transitioning from IBI therapy services to ABA instructional methods in schools. School boards have begun to generalize the multi-disciplinary, team-based model to other transitions (e.g., grade-to-grade, primary to secondary school, etc.) for students with ASD and/or other exceptionalities. The model was fully implemented in all 72 school boards in Ontario in 2010-11. 1,221 children received transition supports through the *Connections for Students* model in 2011-12.

132.007 Sensitivity of Screening Toddlers At Risk of Autism Spectrum Disorders Using M-CHAT Through Mandatory

Health Checkups At 18 and 36 Months in Japan. F. Someki*¹, H. Ito¹, S. Nakajima¹, N. Mochizuki¹, W. Noda¹, N. Takayanagi¹ and M. Tsujii², (1)Hamamatsu University School of Medicine, (2)Chukyo University

Background: Children with autism spectrum disorders (ASD) are known to have varieties of difficulties in their life. Therefore, an effort to detect autism-specific symptoms early and provide children with necessary supports is critical (Robins & Dumont, 2006). Recently, a growing body of literature indicates that children with ASD can be reliably diagnosed as young as age 2 on the basis of various social abnormalities (Kamio, 2009). In Japan, checkups for 18-months-old and 3-year-old toddlers are mandated under the Maternal and Child Health Act starting in 1977, and regional health care centers offer the checkups in the community. In general, checkup areas include physical, dental and language development focusing more on severe/profound disabilities; however, in recent years, many places have started screening milder disabilities such as ASD.

Objectives: The purpose of this study was to examine the sensitivity of screening toddlers with possible ASD using M-CHAT at 18 months by following up the same group of toddlers at 36 months at a regional health care center in Japan.

Methods: This study was a part of an entire cohort study of in a suburban city in Japan. All the 18-months toddlers (N=360) who resided in the city from October 2010 till February 2011 were screened for ASD using the Japanese Version of the Modified Checklist for Autism in Toddlers (M-CHAT) at the mandatory checkup. The same group of toddlers (N=385) came back for the 36-months mandatory checkup from April till August 2012 and were screened using the Pervasive Developmental Disorders Autism Society Japan Rating Scale (PARS: Tani et al., 2009, 2010) for ASD.

Results: Among toddlers who were identified positive for ASD at 18-months, approximately seven percent of them were negative for ASD at 36-months (i.e., false positives), whereas less toddlers were positive for ASD at 36-months for the first time (i.e., false negatives). The authors will add more data at the time of the presentation and present other findings based on the M-CHAT score as well.

Conclusions: In Japan, not many areas introduced the screening of mild disabilities at the mandatory health checkup; therefore, there are not many literatures available that followed up toddlers at risk of ASD longitudinally. The findings may encourage more areas to introduce screeners such as M-CHAT at the mandatory health checkup to intervene toddlers at risk as early as possible.

132.008 Examining Vocational Services for Adults with Autism. D. B. Nicholas*¹, L. Zwaigenbaum², M. Clarke³, J. H. Emery¹ and L. Ghali³, (1)University of Calgary, (2)University of Alberta, (3)Sinneave Family Foundation

Background: The Canadian unemployment rate for persons with disabilities including ASD, is estimated at 53.2% compared to 7.9% in the general population. Redressing this unacceptably low employment rate is of critical importance.

Objectives: We examined types of vocational services offered to adults with ASD, and stakeholders' perceptions regarding risk and protective factors to vocational access 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 telephone survey eliciting vocational models in ASD, (iii) inperson 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 addressing employment support and employer perceptions and needs in establishing sustained work placements for adults with ASD.

Results: Within the province of Alberta, Canada which is home to just under 4 million residents, 75 agencies were identified that offer vocational services to adults with ASD. Interviews and focus groups were conducted with 55 participants, including individuals with ASD, family members, other formal or informal caregivers and vocational service providers. 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. Benefits and limitations of these various approaches are

identified; however, overall vocational services are described to be insufficient to meet current need. 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. Proactive contingency planning and 'in the moment' augmentative support are recommended for possible crises and challenges that may emerge within the workplace. Participants call for a person-centred, targeted and seamless approach to vocational support than is currently offered by most agencies. They recommend core services in job skills and social/relational elements needed in the workplace via core curriculum as well as a corresponding individualized, tailored menu of support that complements individual needs and is intentionally generalizable to the work setting.

Conclusions: Vocational supports are needed, as are sensitive and responsive metrics for evaluation. A 'wraparound' approach is recommended in which individuals with ASD receive initial and fading support and training, along with ad hoc services for the employee and employer, in the possible emergence of problematic issues. HR personnel, employer and policy maker involvement is recommended in building capacity associated with inclusive workplaces. Community advocacy models and periodic assessments of an individual's needs are recommended. These findings posit promising models and recommendations that will be discussed in the presentation. Notwithstanding multiple recommendations, these findings suggest that emerging models offer promise in advancing vocational opportunity for adults with ASD.

Animal Models Program

133 Autism Pathways in Animal Models

Presentations in this session describe results obtained in studies using mouse and rat models of autism. The studies range from defining the neurobiological effects of autism-related gene mutations and environmental insults, to therapeutic interventions, as well as the functional contributions of the cerebellum to the behavioral phenotype.

133.001 Hyperactivity and Abnormal Social and Vocal Behaviours in *ProSAP1/Shank2*^{-/-} Mice, a Model of Autism Spectrum Disorders. E. Ey*¹, C. Leblond², P. Faure³, N. Torquet⁴, A. M. Le Sourd⁴ and T. Bourgeron⁵, (1)*Institut Pasteur*, (2)*Institut PASTEUR*, (3)*CNRS UMR 7102 / Université P. & M. Curie*, (4)*CNRS UMR 2182*, (5)*Paris Diderot University*

Background: Mutations in genes coding for synaptic proteins were shown to increase susceptibility to autism spectrum disorders (ASD). Among the causative proteins, the cell adhesion molecules neuroligins and neuroligins as well as the scaffolding protein *PROSAP2/SHANK3* were repeatedly associated in independent patients with ASD. Recently the scaffolding protein *PROSAP1/SHANK2* has also been associated with ASD and we recently confirmed these results by the identification of novel mutations in patients with ASD and the ascertainment of the functional impact of these mutations on synaptic density (Leblond et al. *PLoS Genetics*, 2012).

Objectives: Following these studies, animal models were developed to better characterise the role of susceptibility genes in ASD. In a collaborative study, we recently analysed transgenic knockout mice lacking *ProSAP1/Shank2* (see accompanying abstract by Schmeisser et al.). These mice display abnormal glutamatergic receptor expression and neurotransmission. Our group investigated the development and the adult behaviour of *ProSAP1/Shank2*^{-/-} mice to understand the contribution of *ProSAP1/Shank2* deletion to symptoms in social, communicative or stereotyped behaviours.

Methods: Comparisons were drawn between *ProSAP1/Shank2*^{-/-}, *ProSAP1/Shank2*^{+/-} and wild-type littermates. Pups and adults were tested to examine the developmental trajectory of abnormalities. We conducted social interactions tests recordings of ultrasonic vocalisations, self-grooming and digging measures, as well as general activity and anxiety measures.

Results: Abnormalities in body weight as well as in vocal behaviour emerged in the first two weeks of life of *ProSAP1/Shank2*^{-/-} pups, and persisted during adulthood. Adult *ProSAP1/Shank2*^{-/-} males and females were hyperactive. Only *ProSAP1/Shank2*^{-/-} females groomed themselves for longer time in comparison with their littermates. Impairments in social interactions emerged mostly in free social interactions, and

appeared together with abnormalities in usage and structure of ultrasonic vocalisations.

Conclusions: All together, this collaborative study suggests that mutations in genes causing ASD in humans can alter glutamatergic neurotransmission and cause alterations in social interactions and communication in mice. Together with other mouse models of ASD, the *ProSAP1/Shank2*^{-/-} mice may provide a comprehensive framework to identify new knowledge-based treatments of ASD.

133.002 Prefrontal Circuitry Deficits in a Novel Shank3-Deficient Rat. J. D. Buxbaum*, M. G. Baxter, O. B. Gunal, H. Harony-Nicolas, P. R. Hof, D. Papapetrou, N. Uppal and F. J. Yuk, *Mount Sinai School of Medicine*

Background: SHANK3 is a critical protein in the postsynaptic density (PSD), which interacts with many synaptic proteins and cytoskeletal elements. Loss of a functional copy of the SHANK3 gene leads to a monogenic form of an autism spectrum disorder (ASD) called Phelan-McDermid Syndrome (PMS). There is good evidence for prefrontal deficits in SHANK3 deficiency and in ASD. Shank3-deficient mouse models, exhibit synaptic dysfunction and behavioral deficits relevant to symptoms of ASD but are not an ideal model for parsing neural circuitry, especially the prefrontal cortex.

Objectives: To further analyze the effect of Shank3 deficiency on neural pathways in brain regions related to ASD symptoms.

Methods: We developed a genetically modified rat model with a targeted disruption of Shank3, choosing a region of the gene relevant to human mutations. We are applying biochemical, electrophysiological, genome wide transcriptional analysis and behavioral studies to reveal changes due to Shank3-deficiency.

Results: We observe reduced levels of Homer and PSD-95 in the hippocampus and medial prefrontal cortex in Shank3-deficient rats. Our results also revealed that reduced levels of Shank3 lead to deficits in hippocampal long-term potentiation (LTP) and long-term depression. Furthermore LTP in the hippocampal-medial prefrontal pathway, analyzed using in vivo recordings of field excitatory responses, was also impaired in

Shank3-deficient rats. Finally, Shank3-deficient rats showed a specific working memory deficit.

Conclusions: By further characterizing this rat model we will be able to reveal disrupted pathways that would then be targets for developing novel therapeutics for PMS and ASD.

133.003 At the Core of Autism: Engineered Models of 16p11.2 CNVs. A. Mills*, *Cold Spring Harbor Laboratory*

Background: Autism is a neurocognitive syndrome characterized by clinical features of repetitive behavior and altered social interactions, as well as a spectrum of co-morbidities such as language impairments, eating problems, and sleep deficits. Copy number variations (CNVs) have been found in patients with autism.

Objectives: The goal of our work is to determine whether 16p11.2 CNVs cause autism-like phenotypes.

Methods: We used chromosome engineering to generate mice with deletion corresponding to 16p11.2—one of the most prevalent genomic lesions associated with autism—as well as mice with reciprocal duplication of this region. We analyzed these 16p11.2 CNV models for behavioral and brain architectural phenotypes using video monitoring and MRI, respectively.

Results: We found that mice with altered dosage of the region corresponding to human 16p11.2 have unique phenotypes, with mice heterozygous for its deletion having neuroanatomical and behavioral phenotypes reminiscent of autism. Deletion mice have repetitive behavior, sleep deficits, and difficulty adapting to a new environment. These behavioral phenotypes correspond with alterations in brain architecture, as MRI and histological analyses define perturbations in specific brain regions. Remarkably, we can identify behavioral alterations just two days after birth, suggesting that these phenotypes can be used as endophenotypes to identify affected children before the full-blown features of autism have developed. Throughout this study, we discovered that deletion causes the most severe phenotype, and that duplication has the reciprocal effect.

Conclusions: These findings provide the first functional evidence that compromised dosage of 16p11.2 is causal in autism-like phenotypes, providing unique models for elucidating the molecular mechanisms involved and for developing new approaches for clinical intervention.

133.004 Autistic-Like Behavior and Cerebellar Dysfunction in Purkinje Cell *Tsc1* Mutant Mice. P. Tsai^{*1}, C. Hull², Y. Chu², W. Regehr² and M. Sahin¹, (1)*Boston Children's Hospital*, (2)*Harvard Medical School*

Background: Autism spectrum disorders are highly prevalent neurodevelopmental disorders, but the underlying pathogenesis remains poorly understood. Although implicated in these disorders, the contribution of cerebellar dysfunction to autism remains unclear. Tuberous Sclerosis is a genetic disorder associated with high rates of comorbid autism.

Objectives: To investigate the cerebellar contribution to autism, we generated a Purkinje cell specific mouse model of Tuberous Sclerosis Complex.

Methods: We generated mice lacking *Tsc1*, one of the genes mutated in Tuberous Sclerosis, in cerebellar Purkinje cells. We examined social interaction, repetitive behaviors, and vocalizations in addition to evaluating cellular and electrophysiologic mechanisms contributing to behavioral phenotypes. Lastly, we treated mice with the mTOR inhibitor, rapamycin, to evaluate whether cellular and behavioral phenotypes could be ameliorated with this therapy.

Results: Homozygous, but not heterozygous, loss of *Tsc1* in Purkinje cells resulted in increased neuronal stress, Purkinje cell loss, and motor deficits. However, both heterozygous and homozygous mutant animals displayed autistic-like behaviors, including abnormal social interaction, repetitive behavior, and abnormal vocalizations, in addition to decreased Purkinje cell excitability. Treatment of mutants with the mTOR inhibitor, rapamycin, prevented both pathological and behavioral deficits.

Conclusions: These findings demonstrate novel roles for *Tsc1* in Purkinje cell function and define, for the first time, a molecular basis for a

cerebellar contribution to cognitive disorders such as autism.

133.005 Abnormal Oxytocin Pathway in the *Cntnap2* Mouse Model of ASD. O. Penagarikano*, M. T. Lazaro, H. Dong, N. P. Murphy, N. T. Maidment, P. Golshani and D. H. Geschwind, *University of California at Los Angeles*

Background:

Genetic, neurobiological and imaging data provide convergent evidence for the *contactin associated protein-like 2 (CNTNAP2)* gene as a risk factor for Autism Spectrum Disorder (ASD) and other neurodevelopmental disorders. The *CNTNAP2* gene encodes for a neuronal transmembrane protein, member of the neurexin superfamily (Poliak et al., 1999), which loss of function has been associated to a syndromic form of ASD called cortical dysplasia-focal epilepsy syndrome (CDFE), a rare disorder resulting in epileptic seizures, language delay, intellectual disability, hyperactivity and, in nearly two-thirds of the patients, autism (Strauss et al., 2006). Mouse models based on human disease-causing mutations provide the potential for understanding gene function and novel treatment development. We have previously demonstrated the construct, face and predictive validity of a mouse knockout for the *Cntnap2* gene (Penagarikano et al., 2011), providing an excellent tool for further studies to unravel ASD pathophysiology and for therapeutic research.

Objectives:

To perform an *in vivo* drug screening in *Cntnap2* mutant mice targeting affected social behaviors.

Methods:

Ten *Cntnap2* knockout mice and wildtype littermates were pharmacologically treated and tested for improvements in social interactions as in Silverman et al. (2010). Immunohistochemistry and receptor binding analysis were performed in four mice per genotype using conventional methods.

Results:

We found that intranasal administration of the neuropeptide oxytocin (OXT) dramatically improves social deficits in this mouse model. Interestingly, the same treatment in wild-type (WT) littermates did not show any behavioral response, suggesting a hyper-reactivity to OXT in *Cntnap2* mice. OXT is synthesized in magnocellular neurons in the paraventricular (PVN) and supraoptic (SON) nuclei of the hypothalamus. It is released both peripherally, where it is involved in diverse physiological functions, and centrally, where it acts as a neuromodulator. Analysis of the expression of *Cntnap2* by *in situ* hybridization shows that it is enriched in the PVN, supporting a role for this gene in the development and/or functioning of these neurons. Interestingly, quantitative PCR from dissected hypothalamus showed that Oxt RNA levels are reduced in *Cntnap2* mutant mice compared to WT and decreased OXT immunoreactivity was found in the PVN of mutant mice. Furthermore, analysis of the distribution of OXT receptors by receptor binding autoradiography shows an abnormal distribution of these receptors in mutant mice comparing to WT littermates.

Conclusions: Several lines of evidence suggest an association of the OXT pathway and ASD, and clinical trials with OXT agonists are underway. Here, we report that the *Cntnap2* mouse model of autism responds to OXT and provide initial evidence that the OXT-OXT receptor pathway is dysregulated in the knockout. Additional work is needed to clarify the neurobiological basis for this deficit and to study the mechanism whereby OXT exerts its behavioral effects.

133.007 Gastrointestinal Symptoms and Probiotic Treatment in a Mouse Model of an ASD Risk Factor. P. H. Patterson*, *California Institute of Technology*

Background: While autism is a neurodevelopmental disorder characterized by language and social deficits, recent studies have highlighted striking dysregulation in the neural, peripheral, and enteric immune systems of autistic individuals. There are also reports that subsets of children with autism spectrum disorder (ASD) display gastrointestinal (GI) abnormalities, including increased intestinal permeability and altered composition of GI microbiota.

Objectives: To explore the potential connections between GI problems and the brain and behavior, we use a mouse model of an ASD risk factor, maternal immune activation (MIA). We also tested the efficacy of probiotic treatment in MIA offspring that display the cardinal ASD behaviors and neuropathology.

Methods: Pregnant mice are injected with poly(I:C) or saline on E12.5. Offspring are fed the probiotic bacteria, *Bacteroides fragilis*, at weaning for one week. Young and adult offspring are assessed for (i) intestinal barrier integrity by measuring leakage of FITC-dextran through the intestinal epithelium and tight junction expression, (ii) GI inflammation by cytokine Luminex array and histology, (iii) serum metabolome profiles by GC-MS and LC-MS.

Results: MIA offspring display decreased intestinal barrier integrity and corresponding changes in levels of tight junction proteins. These symptoms are associated with altered expression of colon cytokines and changes in serum metabolite levels. Postnatal *B. fragilis* treatment ameliorates these GI abnormalities, and normalizes certain serum metabolites and several ASD-related behaviors.

Conclusions: These studies highlight the potential relevance of the gut-brain axis for ASD, where manipulation of the intestinal microbiome can influence GI physiology and behavioral performance. The results raise the possibility of testing a probiotic therapy in individuals with autism and co-morbid GI symptoms. Moreover, the altered serum metabolite profiles in the MIA mouse model raise the possibility of testing particular metabolites as candidate biomarkers for subsets of human ASD.

133.008 Neuroimaging Evidence of Major Morpho-Anatomical and Functional Abnormalities in the BTBR T+TF/J Mouse Model of Autism. L. Doderio¹, F. Sforazzini¹, A. Galbusera¹, M. Damiano¹, S. Tsiftaris², A. Bifone¹, M. L. Scattoni³ and A. Gozzi^{*1}, (1)*Istituto Italiano di Tecnologia Center for Nanotechnology Innovation @NEST*, (2)*IMT - Institutions Markets Technologies, Institute for Advanced Studies Lucca, Italy*, (3)*Istituto Superiore di Sanità*

Background: Autism is a behaviourally defined neuro-developmental disorder of unknown etio-pathology. Human neuroimaging studies have begun to shed light on the neural substrate of this

disorder, by revealing a number of subtle functional and structural alterations which may be related to specific behaviours and symptoms. A strong rationale exists for the extension of this approach to probe and assess the face- and construct-validity of preclinical models for the disorder.

Objectives: The BTBR T+tf/J mouse (BTBR) is an inbred line that shows robust behavioural phenotypes with analogies to all three diagnostics symptoms of autism, including selectively reduced social approach, low reciprocal social interactions and impaired juvenile play. These features have prompted its use as a high face-validity mouse model of autism. However, the extent to which the BTBR model replicates the morpho-anatomical and functional alterations observed in human imaging studies of autism remains unknown. We used a multi-parametric magnetic resonance imaging (MRI) protocol to assess multiple morphoanatomical and functional parameters in the brain of BTBR mice as compared with C57BL/6J (B6) controls.

Methods: Adult male BTBR (N=22) or B6 (N=24) underwent a series of structural and functional MRI scans at 7 tesla. We performed high-resolution white matter (WM) tractography using diffusion tensor imaging (DTI), assessed gray matter volume using voxel-based morphometry (VBM), and measured cortical thickness across strains. Moreover, we measured basal cerebral blood volume (bCBV), an established marker of resting brain function, and resting state functional connectivity using BOLD functional MRI (fMRI).

Results: Intergroup maps of DTI fractional anisotropy using the TBSS method demonstrated the absence of the corpus callosum in BTBR subjects, and highlighted the presence of areas of altered fractional anisotropy in thalamic areas and postero-frontal regions. Tractographic analysis confirmed the lack of inter-hemispheric connections at the level of corpus callosum, forceps minor and dorsal hippocampal commissure and revealed major white matter reorganisation with the presence of major rostro-caudal bundles running alongside the inter-hemispheric cleft. The WM alterations were accompanied by a major reduction of gray matter density in frontal cerebral cortex as seen with VBM and cortical thickness measurements.

Significant alterations in resting state bCBV and functional connectivity were also identified.

Conclusions: Overall, these results highlight dramatic morpho-anatomical and functional abnormalities BTBR mice compared to B6 controls, with a particular involvement of fronto-cortical areas and WM architecture. The magnitude and nature of changes appear to be larger and more substantial than what typically observed in clinical studies, thus questioning the face-validity of the model, at least from a neuroimaging perspective. Our results also highlight the need to identify refined models of ASD capable to reproduce the more subtle functional and anatomical alterations observed in clinical research of autism.

Cognition and Behavior Program

134 Infant Cognition and Behavior

134.001 Decreased Social Attention in 6-Month-Old Infants Later Diagnosed with ASD. K. Chawarska*, S. Macari, D. J. Campbell, S. H. Kim, A. Dowd, K. O'Loughlin, J. Garzarek, G. M. Chen, E. B. Gisin and F. Shic, *Yale University School of Medicine*

Background: The ability to spontaneously attend to the social overtures and activities of others is essential for the development of social cognition and communication. This ability is critically impaired in toddlers with autism spectrum disorders (ASD); however, it is not clear if prodromal symptoms in this area are already present in the first year of life of those affected by the disorder.

Objectives: To examine whether 6-month-old infants later diagnosed with ASD exhibit atypical spontaneous social monitoring skills.

Methods: Visual responses of 67 infants at high-risk (HR) and 50 at low-risk (LR) for ASD were studied using a free-viewing eye-tracking task (Chawarska, Macari & Shic, under review). The stimulus consisted of a 3-minute video of an actress filmed in a setting containing four toys and a table with ingredients for making sandwiches (see Chawarska et al., 2012). The video contained four types of activity (conditions) interspersed with one another, depicting a woman making a sandwich, occasionally looking at the camera and trying to engage the viewer using eye contact and child-directed speech, then going back to the sandwich, or looking at the toys, with

toys sometimes remaining still and sometimes moving. Dwell time on the entire scene, the actress, her face, and objects in the background were recorded. Based on their clinical presentation in the 3rd year, infants were divided into those with ASD, those exhibiting atypical development (HR-ATYP), and those developing typically (HR-TYP, LR-TYP).

Results: Primary hypotheses were tested using linear mixed effects models with group (4) as a between-group factor and condition (4) as a within-group factor. Considering that the task relied heavily on visual discrimination skills and attention to language, individual age equivalents on the Mullen Visual Reception and Receptive Language scales at 6 months were included into the model as covariates. All post-hoc contrasts are reported with a Tukey-Kramer correction for multiple comparisons. Compared to the control groups, 6-month-old infants later diagnosed with ASD attended less to the social scene, and, when they did look at the scene, they spent less time monitoring the actress in general and her face in particular. Limited attention to the actress and her activities was not accompanied by enhanced attention to objects.

Conclusions: Prodromal symptoms of ASD at six months include a diminished ability to attend spontaneously to people and their activities. A limited attentional bias towards people early in development is likely to have a detrimental impact on the specialization of social brain networks and the emergence of social interaction patterns. Further investigation into its underlying mechanisms and role in the psychopathology of ASD in the first year is warranted.

134.002 Atypical Social Attention Patterns in 6-Month-Old Infants Later Diagnosed with ASD During a Face-to-Face Dyadic Interaction. S. H. Kim*, S. Macari, F. Shic, A. Dowd, K. O'Loughlin, J. Garzarek, G. M. Chen, E. B. Gisin and K. Chawarska, *Yale University School of Medicine*

Background: Deficits in spontaneous orienting to naturally occurring social stimuli are one of the defining features of autism in early childhood. Toddlers with autism spectrum disorders (ASD) have been consistently found to show impairments in social attention, but it is not clear if these deficits are already present in the first months of life of those affected by the disorder.

Objectives: The main objective was to examine patterns of social attention during a face-to-face adult-child dyadic interaction in 6-month-old infants who were later diagnosed with ASD compared to infants who did not develop ASD.

Methods: Six-month-old infants (N=94) both at high risk (HR; N=61) and low risk (LR; N=33) for ASD participated in a standardized, live dyadic interaction as part of their participation in a prospective study. Children were assigned a clinical best estimate diagnosis of ASD (11 HR, 2 LR) or non-ASD (including typical development, 25 HR and 31 LR; or non-spectrum delays such as language delays, global developmental delays, 25 HR) in the 3rd year. The face-to-face interaction consisted of five one-minute episodes, graded from purely social interactions (experimenter talking to the infant using motherese, singing a nursery rhyme) to more physical interactions (peek-a-boo, showing a colorful toy, and a tickling game). Attention to various targets (e.g., experimenter's face, experimenter's body, parent, and objects) was coded offline by coders blind to group membership. Patterns of attention were compared using generalized linear mixed models (SPSS GLMM) to examine the effects of diagnostic group and episode.

Results: Infants' targets of attention varied across the five episodes; all infants were able to regulate their attention according to the type of interaction presented. For example, all infants looked at the experimenter's body (her hands) significantly longer during the peek-a-boo episode than during any other episode. However, across all episodes, infants later diagnosed with ASD looked less at the experimenter's face ($F=4.194$, $p<0.05$) and at their parent ($F=4.152$, $p<0.05$), and more at objects ($F=7.216$, $p<0.01$) compared to infants without ASD. Pairwise comparisons revealed main effects of group for attention to face and attention to parent across all episodes. The ASD group attended more to objects than the non-ASD group during the motherese episode only.

Conclusions: At 6 months, infants who were later diagnosed with ASD exhibited a unique pattern of social attention during face-to-face interactions with a stranger. Compared to other non-affected HR and LR infants, 6-month-olds later diagnosed with ASD showed diminished

attention to the social partner as well as to their own parent over the course of the 5-minute probe, and increased attention to objects in the environment, particularly while the examiner spoke to them using motherese. Further investigation into the underlying mechanisms of these prodromal symptoms and their role in the etiology and manifestation of ASD symptoms in the first year of life is needed.

134.004 Sensitivity to Social Contingency in High- and Low-Risk Infants During the First Six Months of Life. S. Glazer*, P. Lewis, A. Klin and W. Jones, *Marcus Autism Center, Children's Healthcare of Atlanta & Emory University School of Medicine*

Background: Typically-developing infants are attuned to the social aspects of their environment, even during the first few months of life. From birth, infants look more at faces and preferentially engage with faces that gaze directly at them. By 3 months, infants are sensitive to the gaze direction of others. In previous research, between 2 and 3 months of age, typically-developing infants also develop sensitivity to social contingencies. Reciprocal social interactions, such as mother-infant face-to-face interactions, play a key role in development of communication and social understanding. Detecting social contingencies is a key milestone in furthering social competency.

Objectives: This experiment is intended to test the hypothesis that changes in visual scanning of infants during face-to-face interactions can act as an indicator of an infants' level of sensitivity to social contingencies. We aim to investigate if differences exist in the level of sensitivity and/or timing of the development of sensitivity to social contingency in typically-developing infants and infants who at high-risk for ASD.

Methods: Using eye-tracking technology, we compared the visual scanning of infants enrolled in a longitudinal prospective study of infant siblings of children with autism spectrum disorder (ASD). Infants at high-risk for ASD (HR-ASD) had a full sibling with a confirmed diagnosis of ASD, whereas infants at low-risk (LR-TDx) had no siblings with, or family history of, ASD. Between ages 2 to 6 months, visual scanning was compared between the two groups during three conditions: watching a videotaped actress (condition 1), participating in face-to-face

interaction with their caregiver (condition 2), and a pre-recorded, thus non-contingent, video of the infant's caregiver recorded during a previous session (condition 3). Dependent measures included each infant's level of fixation on different regions of interest, as well as the timing and duration of those fixations during each experimental condition.

Results: Preliminary data analyzed using a sub-sample of 20 infants (8 LR-TDx and 12 HR-ASD) with a mean age of 3.46 (1.17) months, indicate that during the first 6 months of life infants are sensitive to social contingencies. Infants showed increased levels of fixation during contingent videos (condition 2) as opposed to non-contingent videos (conditions 1 and 3), $t(19) = 3.98, p = .001$. In addition, infants responded differently while participating in face-to-face interactions than while watching pre-recorded videos of an actress or their own caregiver. Our results demonstrate a significant interaction between video type and region of interest ($p = .005$). Post hoc analyses indicate that this effect is driven by increased eye vs. mouth fixation ($F(1,19) = 13.69, p = .002$) and decreased mouth vs. body fixations ($F(1,19) = 5.18, p = .035$) during the face-to-face interactions. Preliminary results showed no difference in our LR-TDx and HR-ASD sub-sample.

Conclusions: Preliminary results suggest that changes in the visual scanning patterns of infants can effectively index infant sensitivity to social contingencies. This experimental paradigm is likely to potentiate between-group differences relative to infants at-risk for autism, thus increasing the utility in detection of early deviations from the normative course of social development.

134.005 Word Segmentation in Infants At High Risk for Autism. D. Beck-Pancer*¹, T. Hutman¹, S. P. Johnson², S. S. Jeste² and M. Dapretto¹, (1)*University of California, Los Angeles*, (2)*UCLA*

Background: Word segmentation –the ability to identify word boundaries in continuous speech– is a fundamental step during language development. Prior research showed that 7-month-olds can identify word boundaries in continuous speech by computing transitional probabilities between syllables (Saffran et al., 1996) and that by 8 months of age, they become increasingly sensitive

to other speech cues (e.g., stress placed on the word-initial syllable) available in the input (Johnson & Jusczyk, 2001). Importantly, early word segmentation has been linked to word learning in 17-month-olds (Graf Estes et al., 2007), as well as to higher vocabulary scores at age two and better language skills in the preschool years (Newman et al., 2006).

Objectives: Given that delayed language development is a hallmark feature of autism, examining word segmentation in infants at high risk for autism may provide a means to detect early abnormalities in the language acquisition process.

Methods: Twenty-eight high-risk and 20 low-risk 9-month-old infants (exposed primarily to English input) participated in this study. During the familiarization phase, infants were exposed to a continuous speech stream created by repeatedly concatenating 4 trisyllabic words. To assess infants' sensitivity to speech cues, a 'stressed' version was created for the first syllable of two words by increasing its duration/amplitude/pitch. Individual syllables and the speech stream were created following the exact same procedures used by Johnson and Jusczyk (2001). Following the familiarization phase, infants' looking times were recorded in response to the presentation of 12 test trials, 3 for each of four test items (blocked and presented in random order): two trisyllabic combinations which occurred 45 times in the speech stream (i.e., 'words' by transitional probabilities) and two trisyllabic combinations which occurred only 15 times in the speech stream but with stress placed on the first syllable (i.e., 'words' by speech cues).

Results: Low-risk infants showed longer looking times for 'words' by the transitional probabilities than for 'words' by speech cues (i.e., the predicted pattern at this age). In contrast, high-risk infants did not show a significant difference in looking times for the two types of words. Furthermore, the proportion of infants who showed longer looking times for 'words' by transitional probabilities vs. speech cues differed significantly in the two groups (80% vs. 45%, respectively). Notably, in the high-risk group, the difference in looking time between 'words' by transitional probabilities and 'words' by speech cues was positively correlated with word comprehension at

18 and 24 months (MacArthur-Bates Communicative Development Inventory), as well as with receptive and expressive language, and verbal mental age at 36 months (Mullen Scales of Early Learning).

Conclusions: Consistent with prior findings, low-risk infants showed evidence of segmenting the speech stream by relying on the speech cues available in the input. As a group, high-risk infants did not show this pattern; however, the extent to which these infants showed looking time differences in the expected direction predicted better language skills at 18, 24, and 36 months. These findings suggest that word segmentation may aid in the early identification of autism.

134.006 Patterns of Temperament Development in Infants Who Develop ASD. S. Paterson*¹, A. Estes², B. M. Winder³, C. Gilman⁴, H. Gu⁵, L. Zwaigenbaum⁶ and T. IBIS Network⁷, (1)Children's Hospital of Philadelphia, (2)University of Washington, (3)Bryn Mawr College, (4)The Children's Hospital of Philadelphia, (5)University of North Carolina - Chapel Hill, (6)University of Alberta, (7)University of North Carolina- Chapel Hill

Background: Studies suggest young children with autism spectrum disorders (ASD) may exhibit extremes of temperament early in development (Gilbert et al., 1990). Prospective studies of infants at high risk for ASD are inconclusive, reporting increased passivity in HR infants at 6 months, less surgency, or no clear differences (Zwaigenbaum et al., 2005; Clifford et al., 2012; Bolton et al., 2012). Research is needed to determine whether the standard constructs used to measure temperament in normative populations (i.e., the IBQ-R, Gartstein & Rothbart, 2003) are applicable to infants at risk for ASD. It is possible differences in IBQ factor scores may mask true differences in the temperament profile of young children at risk for ASD.

Objectives: We aim to characterize temperament in a longitudinal cohort of infants at high risk for autism. We will evaluate whether standard measures of temperament adequately fit data from infants at high risk for ASD.

Methods: Two hundred and seventy-three infants with older siblings with ASD (HR) and 150 infants with typically developing older siblings (LR) were assessed at 6, 12, and 24 months as part of a larger, multi-site, study of brain and behavioral

development in ASD, the Infant Brain Imaging Study. Temperament was assessed at 6 and 12 months using the IBQ-R. Autism symptoms were assessed at 24 months using the ADOS. Preliminary data from a subset of infants from one clinical site is reported here (HR n=45, LR n=12). The full sample will be used for the final analysis. We will use standard factor scores (Surgency, which encompasses approach behaviors, Regulatory control, and Negative Affect) and subscales from the IBQ-R to compare HR vs LR infants, and will use ADOS scores to form groups based on ASD symptoms. We will then perform a factor analysis to examine whether the standard three factor solution adequately fits data gathered from this large, HR infant cohort.

Results: Infants from the smaller subset were grouped according to 24 month outcome using ADOS cut off scores (HR ASD positive, HR ASD negative, LR ASD negative). Using one-way ANOVA, no differences were found in 6 month factor scores. At 12 months, Surgency was significantly reduced for the HR ASD positive group, $F(2,57) = 4.73, p < .05$. At 6 months, subscales revealed group differences on Smiling and Laughter, $F(2,56) = 4.986, p < .01$, Low Pleasure $F(2,56) = 5.628, p < .01$, and Vocal Reactivity $F(2,56) = 3.776, p < .03$. At 12 months, group differences were found on Smiling and Laughter $F(2,57) = 7.213, p < .01$, and Vocal Reactivity, $F(2, 57) = 7.479, p < .01$. We will examine these differences in the larger group of infants and conduct factor analyses on this larger data set.

Conclusions: Preliminary analyses suggest that infants who develop ASD at 2 years of age may smile and vocalize less than HR ASD negative and LR ASD negative infants. Despite no factor-level differences at 6 months, subscale analyses do reveal group differences at this age. Future research is needed to investigate whether alternative measurement strategies may better characterize temperament in infants at high risk of ASD.

134.007 Quality of Interaction Between At-Risk Infants and Caregiver At 12-15 Months Is Associated with 3-Year Autism Outcome. M. W. Wan^{*1}, J. Green¹, M. Elsabbagh², M. H. Johnson³, T. Charman⁴ and .. The BASIS Team⁵, (1)University of Manchester, (2)McGill University, (3)Birkbeck, University of London, (4)Institute of Education, (5)BASIS

Background: Recent models of the early emergence of autism spectrum disorder (ASD) propose that infant intrinsic risk susceptibilities in behaviour may be amplified by interaction within the early social environment into an increasingly atypical developmental trajectory. A few studies have examined prospectively parent-infant interaction in infants who have an older sibling with ASD ('at-risk siblings') and found specific differences from those in low-risk controls, but studies have involved small samples, findings have been inconsistent and there has been little follow-up to later ASD outcome.

Objectives: This study examined whether 6- and 12-month parent-infant interactions in at-risk siblings differ from those with low-risk, and whether – in at-risk siblings – such interactions predict later 3-year classification of ASD, or no ASD.

Methods: Within the British Autism Study of Infant Siblings (BASIS), 6-min videotaped episodes of parent-infant free play in infants at 6-10 months ('6 months': 45 at-risk siblings, 47 low-risk siblings) and 12-15 months ('12 months': 43 at-risk siblings, 48 low-risk siblings) in a laboratory setting were rated on the *Social Interaction Measure for Parents and Infants* (SIM-PI), blind to participant information. Standard tests were administered for concurrent behavioural signs of ASD features and developmental level. Systematic consensus diagnostic classification of ASD was made at 3 years for the at-risk siblings.

Results: Parent non-directiveness and sensitive responsiveness differed in relation to ASD/risk status (at-risk ASD, at-risk no-ASD, low-risk) at both 6 and 12 months. At 6 months, infant liveliness was lower in the high-risk groups; at 12 months, infant attentiveness to parent and positive affect were lower in the at-risk group later diagnosed with ASD. Dyadic mutuality and intensity of engagement showed a group effect at 12 months. Dyadic mutuality, infant positive affect, and infant attentiveness to parent at 12 months (but not 6 months) predicted 3-year ASD outcome, whereas infant ASD-related behavioural atypicality did not.

Conclusions: This is the first prospective evidence that early dyadic interaction between at-risk infants and their parents is associated with later

diagnostic outcome in ASD. Possible explanations for these findings and their theoretical implications are considered.

134.008 Behavioural Risk Markers for Autism in Early and Later Infancy: A Prospective Study of High-Risk Siblings Using the Autism Observation Scale for Infants. I. Gammer*¹, K. R. Davies², H. Ribeiro², L. A. Tucker², A. Volein², H. Garwood², M. Elsabbagh³, G. Pasco¹, M. H. Johnson², T. Charman¹ and .. The BASIS Team⁴, (1)Institute of Education, (2)Birkbeck, University of London, (3)McGill University, (4)BASIS

Background: The British Autism Study of Infant Siblings (BASIS) is a longitudinal study involving participants with older siblings with a diagnosis of ASD (high-risk sibs) and controls with older siblings with no family history of ASD. Participants are assessed at four points between 6 and 36 months, using a range of observational, experimental and questionnaire measures. The Autism Observation Scale for Infants (AOSI) is an experimenter-led, standardized assessment of 19 putative early risk markers for ASD, developmentally appropriate for infants aged between 6 and 18 months. Item codes can be summed to yield a *Total Score*, or non-zero codes counted to yield a *Number of Markers*.

Objectives: To assess whether individual items, total AOSI scores or cumulative AOSI scores (summed across two time points) differ between risk or outcome groups.

Methods: Fifty-four high-risk infants and 50 low-risk controls took part in the study. The AOSI was administered at two visits when infants were aged around 7 months ($M = 7.4$, $SD = 1.26$), and 14 months ($M = 13.8$, $SD = 1.46$). Based on information from later assessments at around 24 and 36 months, high-risk infants were assigned to one of three outcome groups: Sibs-ASD ($n=17$) who received a best-estimate clinical diagnosis of ASD; Sibs-AT ($n = 12$) who were considered not to be typically developing, but who did not meet criteria for ASD; Sibs-TD ($n=24$) who were considered to be typically developing.

Results: After controlling for IQ, higher AOSI *Number of Markers* but not *Total Score* differentiated high-risk sibs from low-risk controls at both the 7 and 14 month visits. Higher cumulative scores on both measures differentiated the high-risk group from controls, irrespective of IQ. Both *Number of Markers* and *Total Score* were

significantly higher in the Sibs-ASD group compared to controls at the 14 month visit, but not the 7 month visit, although these differences did not remain significant after controlling for IQ. Higher *Cumulative Number of Markers* differentiated Sibs-ASD from controls irrespective of IQ. At the 7 month visit higher scores on *Social Referencing* differentiated Sibs-ASD from controls and two further items (*Visual Tracking* and *Motor Control and Behaviour*) differentiated Sibs-AT from controls. Cumulative item scores yielded more significant item-level differences than scores from either single visit.

Conclusions: Findings contribute towards the validation of the use of the AOSI to detect risk of ASD and provide some evidence of behavioural differences from as early as 7 months. Summing scores from multiple time points across infancy improves the capacity of the AOSI to identify those at highest risk and appears to provide a more robust measure, consistently differentiating risk and outcome groups irrespective of IQ.

Cell Biology Program

135 Cell Biological Mechanisms

135.001 1 Relationship Between Decreased Activity of Protein Kinase C and Behavioral Abnormalities in Regressive Autism. V. Chauhan*¹, L. Ji² and A. Chauhan², (1)NYS Institute for Basic Research In Developmental Disabilities, (2)NYS Institute for Basic Research in Developmental Disabilities

Background: Autism is a neurodevelopmental disorder with unknown etiology. In some cases, typically developing children regress into clinical symptoms of autism, a condition known as regressive autism. The cause of regression in autism is not understood. Protein kinases are known to play important roles in cellular signaling pathways, and are involved in neurodevelopment, neuronal functions, gene expression, memory, and cell differentiation. The brain synapses are the building blocks of memory formation, and synaptic strength contributes to learning and memory.

Objectives: Recently, we reported decreased activity of protein kinase A (PKA) in the frontal cortex of subjects with regressive autism. In this study, we analyzed the activity of protein kinase C (PKC) in the cerebellum and different regions of cerebral cortex from subjects with regressive

autism, autistic subjects without clinical history of regression, and age-matched control subjects.

Methods: The postmortem frozen brain regions, i.e., cerebellum, and cortices from frontal, temporal, parietal and occipital regions of brains from autism and control subjects were obtained from NICHD Brain and Tissue bank for Developmental Disorders at the University of Maryland. The tissues were homogenized (10% w/v) in cold buffer containing 50 mM Tris-HCl (pH 7.4), 8.5% sucrose, 2 mM EDTA, 10 mM b-mercaptoethanol and protease inhibitor cocktail in a Downs homogenizer with 5 strokes at 4 °C. The protein concentration was assayed by the Bradford method. Activity of PKC was measured by enzyme linked-immunosorbent assay kits.

Results: In the frontal cortex of subjects with regressive autism, PKC activity was significantly decreased by 57.1% as compared to age-matched control subjects ($p = 0.0085$), and by 65.8% as compared to non-regressed autistic subjects ($p = 0.0048$). PKC activity was unaffected in the temporal, parietal and occipital cortices, and in the cerebellum in both autism groups, i.e., regressive and non-regressed autism as compared to control subjects. These results suggest brain region-specific alteration of PKC activity in the frontal cortex of subjects with regressive autism. Analysis of correlation between PKC activity and behavior parameters of subjects with autism showed a negative correlation between PKC activity and restrictive, repetitive and stereotyped pattern of behavior ($r = -0.084$, $p = 0.0363$) in autistic individuals, suggesting involvement of PKC in behavioral abnormalities in autism.

Conclusions: These findings suggest that regression in autism may be attributed, in part, to alterations in G-protein-coupled receptor-mediated signal transduction involving PKA and PKC in the frontal cortex.

135.002 2 Non-Protein-Bound Iron and 4-Hydroxynonenal Protein Adducts in Autistic Spectrum Disorders. R. Canitano¹, A. Pecorelli², S. Leoncini², C. De Felice³, C. Signorini², G. Valacchi⁴, L. Ciccoli² and J. Hayek^{*3}, (1)University hospital of Siena, (2)University of Siena, (3)University Hospital of Siena AOUS, (4)University of Ferrara

Background: A potential relationship between oxidative stress (OS) and autism spectrum disorders (ASDs) has been repeatedly explored,

nevertheless, the OS contribution in the autism pathogenesis is still not fully elucidated

Objectives: to evaluate the redox status in ASD

Methods: In this study we investigated for the first time the levels of non-protein-bound iron (NPBI), a pro-oxidant factor, and 4-hydroxynonenal protein adducts (4-HNE-PAs), as a marker of lipid peroxidation-induced protein damage, in children with ASD ($n=20$, mean age 12.0 ± 6.2 years).

Results: Intraerythrocyte and plasma NPBI levels measured by HPLC result significantly increased (1.98- and 3.56-folds) in patients with ASD, as compared to controls ($n=18$, mean age 11.7 ± 6.5 years) ($p=0.0019$ and $p<0.0001$, respectively). Likewise, immunoblotting analysis shows significantly higher levels of 4-HNE PAs in erythrocyte membranes and in plasma (1.58- and 1.6-folds, respectively) from patients with ASD ($p=0.0043$ and $p=0.0001$, respectively). Antioxidant erythrocyte GSH was slightly decreased (-10.34 %) in patients ($p=0.0215$).

Conclusions: Our findings indicate an impairment of the redox status in ASD patients, with a pro-oxidant / antioxidant balance shifted toward the pro-oxidant arm. Increased levels of NPBI could contribute to lipid peroxidation and, consequently, to increased plasma and erythrocyte membranes 4-HNE-PAs, thus amplifying the oxidative damage, potentially contributing to the phenotype of AD.

135.003 3 Dysfunctional BDNF/TrkB/PI3K Signaling in Autism Disrupts Intracellular Pathways Regulating Spine Protein Synthesis and Dynamics. C. Nicolini^{*1}, F. Haque¹, E. Menna², M. Matteoli², P. Szatmari³, E. Tongiorgi⁴ and M. Fahnstock¹, (1)McMaster University, (2)University of Milano, (3)Offord Centre for Child Studies & McMaster University, (4)University of Trieste

Background: Impairments in cortical connectivity are a hallmark of autism and account for cognitive and behavioural deficits of autistic patients. Both aberrant spine protein synthesis and disrupted remodeling of actin cytoskeleton may affect spine formation, stabilization, size and density, thereby resulting in synaptic dysfunction and perturbed neuronal circuit development. Local protein synthesis and actin reorganization at synapses are regulated by intracellular signaling cascades

triggered by BDNF/TrkB-mediated activation of PI3K. We previously demonstrated imbalances in BDNF and TrkB isoforms and decreased Akt protein in postmortem brain tissue of subjects with autism compared to controls.

Objectives: To investigate whether BDNF/TrkB-activated intracellular cascades, PI3K-Akt-mTOR, involved in spine protein synthesis, and PI3K-Eps8-Rac, regulating synapse formation, are disrupted in autism.

Methods: We examined p70S6K, an mTOR downstream effector which can be taken as a measure of altered mTOR-mediated protein synthesis, and Eps8, a signaling protein that is part of a trimeric complex which links BDNF-mediated PI3K activation to Rac-induced remodeling of actin cytoskeleton at synapses. We also assayed protein expression of Erk1/2, a signaling molecule activated by BDNF/TrkB, the synaptosomal protein SNAP-25 and the pan-neurotrophin receptor p75NTR which signals through the Rac-Rho pathway. Protein was examined by Western blotting in postmortem fusiform gyrus of autism and control subjects.

Results: Significantly decreased p70S6K and Eps8 protein levels were found in fusiform gyrus of subjects with autism compared to controls. No significant difference in Erk1/2 or SNAP-25 protein expression was measured in autism compared to control tissue. Lastly, a trend towards increased p75 receptor was observed in autism subjects compared to controls.

Conclusions: Both reduced p70S6K and Eps8 protein levels are consistent with the down-regulation of the BDNF/TrkB signaling pathway that we previously demonstrated in fusiform gyrus of autistic subjects compared to controls. This suggests disruption of spine protein translation through p70S6K and remodeling of the actin cytoskeleton through Eps8 at synapses. Dysregulation of spine dynamics and densities is further supported by the trend towards elevated p75 receptor in autism which is consistent with increased proBDNF protein we observed in autism compared to control tissue, and likely affects regulation of spine dynamics and density via Rac/Rho. Since changes in spine protein translation, dynamics and stability due to dysfunctional BDNF/TrkB/p75 signaling may alter

cortical connectivity, the balance between excitatory and inhibitory currents, and synaptic plasticity and function, abnormalities at spines may be the underlying biological mechanism responsible for autism core symptoms.

135.004 4 Faecal Fermentation Products and Microbiota Are Altered in Children with Autism Spectrum Disorder. M. T. Angley*¹, L. Wang¹, C. T. Christophersen², M. J. Sorich¹, C. P. Gerber¹ and M. A. Conlon², (1)University of South Australia, (2)CSIRO Food and Nutritional Sciences

Background:

Autism spectrum disorder (ASD) is a complex neurodevelopmental condition and recent studies have implicated gastrointestinal (GI) factors. Evidence is emerging that the profiles of the GI microbiota (Song et al. 2004; Finegold et al. 2010) and fermentation products (Yap et al. 2010) in individuals with ASD are different from those without ASD. Finegold et al. (2002) have reported a relationship between regressive autism and altered GI microbiota. Williams et al. (2012) found intestinal biopsy samples from more than half of children with ASD and GI disturbance (ASD-GI) were PCR positive for *Sutterella* compared with none of a control group (CON-GI). Further, the modulation of intestinal microbiota in children with ASD through the use of probiotics such as *Lactobacillus plantarum*WCSF1 has been shown to improve behaviour and bowel health outcomes (Parracho et al. 2010). Large bowel fermentation products, such as short chain fatty acids (SCFAs), phenols and ammonia, can have beneficial or detrimental effects on health and can contribute to various physiological and neurological processes. Studies conducted by MacFabe and colleagues in rats (2007; 2008) have shown that intraventricular administration of propionic acid induced behaviours resembling ASD and reproduced the neuropathological changes reported to occur in ASD.

Objectives:

- 1) To measure fermentation products in faeces of children with and without ASD to examine whether there is an underlying disturbance in fermentation processes in the disorder.
- 2) To measure relative abundances of various GI bacteria, including *Clostridium* species, members

of the *Bacteroides fragilis* group, *Akkermansia muciniphila*, *Prevotella* species and *Sutterella* species, which are emerging as important markers of GI health.

Methods:

Faecal samples (48 h) were collected from children with autism (n=23, ASD), siblings (n=22, SIB) and community controls (n=9, CON). Faecal concentrations of carbohydrate and protein fermentation products, including SCFA, ammonia, phenol and p-cresol, were measured. Total faecal bacterial DNA was isolated and used for estimating numbers of selected bacterial species using quantitative real-time PCR

Results:

There were significant increases in faecal concentrations of total SCFAs and propionic acid in children with ASD compared to community controls. Moreover, a higher ammonia level appeared in children with ASD than siblings. In addition, lower relative abundances of *Bifidobacteria* species and the mucolytic bacterium *Akkermansia muciniphila* were shown in the faeces of children with ASD compared to controls (SIB and CON). Further, there was a higher faecal abundance of *Sutterella* species found in children with ASD compared with community controls.

Conclusions:

These findings indicate that gut microbiota and fermentation processes are altered in children with ASD. Since fermentation and microbial activity are influenced by diet, food selection and/or probiotic interventions may be important in managing ASD if such changes contribute to the phenotypic presentation of the disorder.

135.005 5 Anti-Phospholipid Antibodies in Autism Spectrum Disorders. M. Careaga^{*1}, R. Hansen², I. Hertz-Picciotto², J. Van de Water² and P. Ashwood¹, (1)University of California, Davis, (2)The M.I.N.D. Institute, University of California, Davis

Background: Autism spectrum disorders (ASD) are etiologically complex and heterogeneous, and in many cases are thought to involve the interplay of genetic and environmental factors. Growing evidence suggests that immune dysfunction may

play a role in ASD, including the presence of specific autoantibodies in both mothers and their affected children. Diverse targets have been suggested for these antibodies, ranging from neuronal targets to yet uncharacterized proteins. However, most studies have had inconsistent findings and there are few studies that have replicated any specific antigenic target. In adults Anti-phospholipid antibodies are associated with cognitive, neuropsychiatric, and neuromotor impairments; however, little is known about their role in pediatric cases or their levels in ASD.

Objectives: In the current study, we investigated whether there were elevated levels of anti-phospholipid antibodies in the plasma of young children with ASD compared to age matched typically developing (TD) controls and children with developmental disabilities (DD) other than ASD.

Methods: Plasma was isolated from acid-citrate dextrose Vacutainers and was assessed by commercial ELISA for antibody levels of anti-Cardiolipin, anti-Phosphoserine, and anti-β2-Glycoprotein 1 antibodies. Participants included 54 children with ASD [median age 44.8 months (interquartile range 32.0–57.7), 45 males], 33 TD controls [40.6 months (27.7–53.6), 27 males] and 22 DD controls [41.7 months (25.7–57.8), 18 males].

Results: Antibody levels for anti-Phosphoserine ($p < 0.01$), and anti-β2-Glycoprotein 1 ($p < 0.001$) were found to be significantly higher in children with ASD compared with TD and DD controls. Antibody levels of anti-Cardiolipin were significantly higher compared with TD controls ($p < 0.001$), and although there was a trend to elevated levels in children with ASD compared with DD controls, this did not reach statistical significance after multiple correction. In addition, increased levels of anti-phospholipid antibodies were found to associate with more severe behavior impairments as measured by the Aberrant Behavior Checklist (ABC), Mullen Scales of Early Learning (MSEL), and Vineland Adaptive Behavior Scales (VABS).

Conclusions: We found that levels of anti-Cardiolipin, β2-Glycoprotein 1, and anti-Phosphoserine antibodies were elevated in children with ASD compared with age matched TD

and DD controls. The increase in antibody levels was associated with impaired behaviors on the ABC or decreased cognitive and adaptive functions on the MSEL and VABS. This study provides evidence for the production of anti-phospholipid antibodies in young children with ASD, as these antibodies have previously been associated with neuropsychiatric impairments, and suggests a unique avenue for investigation of potential future therapies in ASD.

135.006 6 Autism and Phthalate Metabolite Glucuronidation. X. Ming^{*1}, T. P. Stein², M. D. Schluter² and R. A. Steer², (1)UMDNJ-New Jersey Medical School, (2)UMDNJ-School of Osteopathic Medicine

Background: Exposure to environmental chemicals (ECs) may precipitate Autism Spectrum Disorders (ASD) in genetically susceptible children. Differences in the efficiency of the glucuronidation process may substantially modulate substrate concentrations and effects.

Objectives: To determine whether the efficiency of this pathway is compromised in children with ASD.

Methods: We measured the efficiency of glucuronidation for a series of metabolites derived from the commonly used plasticizer, Diethylhexyl phthalate (DEHP). DEHP is first hydrolyzed to mono-2-ethylhexyl phthalate (MEHP) and then further metabolized by a series of oxidation reactions to mono-(2-ethyl-5-oxohexyl) phthalate (5-oxo MEHP), mono-(2-ethyl-5-hydroxyhexyl) phthalate (5-OH MEHP) and mono-(2-ethyl-5-carboxypentyl) phthalate (5-cx MEPP) which are then glucuronidated. We compared the efficiency of glucuronidation for conjugation in 50 children with ASD and against 53 controls. Spot urines were collected and analyzed for the fraction of each metabolite conjugated by isotope dilution-liquid chromatography mass spectrometry-mass spectrometry.

Results: Conjugation capacity was consistently lower with the ASD group based on both the median and adjusted mean values of OH-MEHP and 5-oxo MEHP in each group. There was a statistically significant correlation between the fractions 5-OH MEHP conjugated with 5-oxo-MEHP ($r = .51$, $P < .001$) suggesting a common pathway.

Conclusions: The glucuronidation pathway is compromised in some children with ASD. Because the glucuronidation pathway is responsible for the detoxification of many compounds, which one(s) are compromised in ASD cannot be said at this time.

Neurophysiology Program

136 Neurophysiology 2

136.009 9 Specificity of Atypical Neural Development for Language in Infants At Risk for ASD. P. Hashim^{*1}, M. Coffman², C. E. Mukerji², R. Tillman², D. Perszyk², J. S. Turner³, R. Travieso⁴, N. Landi⁵, L. Mayes², J. A. Persing¹ and J. C. McPartland², (1)Yale University School of Medicine, (2)Yale Child Study Center, (3)Montefiore Medical Center, (4)Duke University School of Medicine, (5)Haskins Laboratories

Background:

While difficulties in communication are characteristic of autism spectrum disorders (ASD), it remains unclear whether the observed language delays are intrinsic to language processing abilities or develop secondary to social deficits. Non-syndromic craniosynostosis (NCS) and deformational plagiocephaly are craniofacial conditions resulting in abnormal head shape that have also been associated with atypical language development. NCS occurs as the result of premature fusion at one or more skull growth sites and affects roughly 1 in 2000 live births. Deformational plagiocephaly, which affects as many as 48% of infants, is caused by mechanical forces acting on the head in utero or by postnatal positioning. Despite shared difficulties, there has been no study to date comparing atypical neural development in ASD and conditions of cranial asymmetry.

Objectives:

Given recent evidence that infants at high risk for ASD demonstrate atypical perceptual narrowing (Seery et al., 2010), this study aimed to examine language processing in infants at high risk for ASD relative to those with NCS or deformational plagiocephaly. Our goals were to elucidate the underlying processes behind language delay in ASD through comparison to (a) other conditions of atypical cognitive development and (b) normal-risk infants.

Methods:

Three groups of infants under 12 months participated in the study: 15 infants at high risk for ASD by virtue of having a sibling diagnosed with the disorder, 15 normal-risk controls, and 40 infants previously diagnosed with NCS or deformational plagiocephaly. ERPs were recorded with a 128 channel HydroCel Geodesic Sensor Net during auditory presentations of native (English) and non-native (Hindi) phonemes. ERP analysis focused on the mismatch negativity (MMN) recorded over the midline scalp.

Results:

Consistent with predictions, control infants displayed a robust MMN between 6 and 9 months, indicating differentiation of native and non-native phonemes (mean difference= 3.56 microvolts). Analyses in progress contrast MMN amplitude between these normal-risk controls, infants at high risk for ASD, and non-ASD risk infants. We predict that subjects from ASD and non-ASD risk conditions will demonstrate persistent discrimination of the non-native phoneme at later ages relative to normal-risk subjects, indicating deviant or delayed language processing.

Conclusions:

Results will provide insight into the contributory mechanisms of language impairment in ASD. By examining the degree of deficient intrinsic language processing, our study will help to clarify the development of communicative delay in ASD. Because prior research in the neural development of infants at risk for ASD has lacked non-ASD clinical groups, this study will provide critical information regarding the specificity of atypical developmental patterns in ASD.

136.010 10 Processes of Risk and Resilience in the Developing Brain: Evidence From Infants At-Risk for Autism. M. Elsabbagh^{*1}, E. Mercure², K. Hudry³, G. Pasco⁴, T. Charman⁴, A. Pickles⁵, M. H. Johnson² and .. The BASIS Team²,
(1)McGill University, (2)Birkbeck, University of London,
(3)La Trobe University, (4)Institute of Education, (5)Institute of Psychiatry

Background: While the focus of infant siblings research has traditionally been to identify early risk markers for diagnosis of autism, we

previously proposed that some early differences may reflect "canalization, i.e. spontaneous correction of developmental pathways following early expression of risk.

Objectives: Our goal was to examine whether eye gaze processing in infants at-risk predicts autism diagnosis at three years of age. Furthermore, we characterize processes of risk and resilience in the infant brain at 6-months for the entire group of infants at-risk that go on to develop variable outcomes in toddlerhood. We use a data-driven approach to ascertain whether event-related potential (ERP) findings fit with hypothetical profiles corresponding to a range of outcomes including canalization.

Methods: Participants were from the British Autism Study of Infant Siblings (BASIS). One hundred infants (54 high-risk sibs and 50 low-risk controls) were included in the analysis. When aged between 6 and 10 months, ERPs were recorded while the infants viewed various gaze and face contrasts. Outcome measures at 2- and 3-years of age included a range of standardized measures combined with expert clinical judgment to ascertain outcome classification.

Results: Atypical response to gaze shifts at 6-months characterized the group that went on to develop autism at 3-years of age. This is the first study to demonstrate that subtle signs observed within the first year of life are associated with emerging behavioral symptoms of autism in toddlerhood.

On the whole, relative to the control group, the high-risk siblings group showed both similarities and differences in the amplitude and latency of components related to gaze processing. However, within the high-risk group, the variation in individual infant's ERP response characteristics was associated with variable outcome measures. Atypical response to static gaze characterized the group of infants at-risk who went on to exhibit typical outcomes. On several additional measures, the three groups were indistinguishable.

Conclusions: As a group, infants at-risk for autism show differences in certain neural components related to the processing of face and gaze. Moreover, individual differences in the infant ERP

could be mapped onto behavioral characteristics of the same infants when they reach toddlerhood. The findings help to highlight the potential scientific and clinical utility of infant ERP measures. Specifically, we propose three hypothetical profiles as targets for future research with infant siblings. Infants within the first year of life may exhibit risk markers that are (a) compounded and amplified over time leading to cascading effects across multiple domains of functioning and a diagnosis, (b) expressed subtly and remain stable leading to characteristics of the broader autism phenotype, or (c) canalized through influences of protective genetic and/or environmental factors leading to typical behavioral outcome.

136.011 11 Electrophysiological Correlates of Speech Perception in 9 Month Olds At Risk for ASD. A. Seery*¹, H. Tager-Flusberg¹ and C. A. Nelson², (1)*Boston University*, (2)*Boston Children's Hospital*

Background: Between 6 and 12 months, typically-developing infants undergo a process of perceptual narrowing where they lose the ability to perceive the phonemic contrasts that are not used in their native language (e.g., Werker & Tees, 1984; Rivera-Gaxiola, Silva-Pereyra, & Kuhl, 2005). Our recent ERP work suggests that infants who are at a high risk for developing ASD (HRA; at risk due to having an older sibling with a diagnosis) do not necessarily appear delayed in undergoing this perceptual narrowing. However, it is possible that infants who ultimately develop ASD show a different trajectory, especially since the process may depend on social engagement with a speaker.

Objectives: Here, we collected ERP to speech sounds in order to study perceptual narrowing in 9-month-old infants at risk for ASD. Importantly, we expanded an original sample substantially, allowing us to again examine our original finding of no delay in the HRA group in addition to looking more closely at the 20% of HRA infants who we expect to ultimately develop ASD.

Methods: We collected ERP while using a double-oddball paradigm to present infants with a stream of three consonant-vowel speech sounds: a standard (presented 80% of the time), a non-native deviant (10%), and a native deviant (10%). In this sample, we included data from 127 9-month-old infants (60 HRA and 67 LRC); to

date, 7 of the HRA infants have received a diagnosis of ASD (4 confirmed through clinical review at 36 months; 3 suspected due to symptoms at 18 or 24 months).

Results: We used a repeated-measures 3x2x2 ANOVA (condition x hemisphere x group) to examine the maximum amplitude of a linguistic ERP component, the P150, over frontal electrodes in HRA versus LRC infants. This revealed a main effect of condition ($F(2,250)=9.603$, $p<.001$), as expected from our previous work. Specifically, the P150 amplitude was larger to both the native (average maximum amplitude=7.48 μ V) and non-native (6.49 μ V) deviants than to the standard (5.30 μ V; $p<.05$ for both paired comparisons). Critically, there was no main effect of or interaction with group (both $p>.6$). However, we found a somewhat different pattern of response in the group of infants with a positive ASD diagnosis. In these infants, we found no difference in the P150 amplitudes of the three stimuli (standard: 7.44 μ V, native: 7.79 μ V, non-native: 6.41 μ V).

Conclusions: Our data suggest that 9 month olds at risk for ASD, as a group (most of whom will not be diagnosed with ASD), do not differ from typically-developing infants in their phonemic perceptual narrowing (at least as measured by P150 amplitude). However, looking at this component specifically in the infants who do ultimately develop ASD (although the group size is relatively small), we found preliminary evidence for a lack of sensitivity to the type of speech sound that was presented. Future work will investigate this finding more closely and will examine possible factors, such as attention, that might contribute to it.

136.012 12 Neural Sensitivity to Biological Motion Versus Audio-Visual Synchrony in Infants At Risk for Autism. R. Tillman*¹, M. Rolison², G. Righi¹, C. E. Mukerji¹, A. Naples¹, M. Coffman¹, J. H. Foss-Feig³, P. Hashim⁴ and J. C. McPartland¹, (1)*Yale Child Study Center*, (2)*Autism Science Foundation*, (3)*Yale University*, (4)*Yale University School of Medicine*

Background: Perceptual sensitivity to biological motion is critical to social function and present from birth. Detection of temporal contingency between auditory and visual events is also a key developmental ability evident in infancy. Behavioral studies suggest a potentially

maladaptive imbalance in these early developing skills in autism spectrum disorder (ASD); toddlers with ASD display preferential attention to audio-visual synchrony (AVS) rather than the typical preference for biological motion. Researchers have not yet investigated the neural bases for an insensitivity to biological motion or a hypersensitivity to AVS in infants at high-risk (HR) for ASD.

Objectives: The present study measured electrophysiological brain responses to biological motion and AVS in infants at HR and normal-risk (NR) for ASD. By contrasting biological markers for human motion and temporal contingency of audio-visual stimuli, we aimed to detect (a) undersensitivity to biological motion and (b) oversensitivity to AVS in order to characterize indicators of atypical social development prior to the emergence of behavioral symptoms.

Methods: Participants included HR (n=20) and NR (n=40) infants assessed longitudinally at three-month time points between 3 and 18 months of age. EEG was recorded with a 128-channel Hydrocel Geodesic Sensor net while infants were presented with: point-light displays depicting biological motion and non-biological (scrambled) motion (Experiment 1); or unimodal and bimodal auditory (tone) and visual (circle) stimuli (Experiment 2). In Experiment 1, event-related potentials (ERPs) evoked by biological or scrambled motion and event-related oscillations (EROs) in the mu range (6-9 Hz), indexing activity in the action perception system, were extracted. In Experiment 2, ERPs evoked by unimodal and bimodal stimuli presentations and EROs in the gamma range (20-100 Hz), indexing binding and feature integration mechanisms, were extracted. All infants were administered the Mullen Scales of Early Learning and a comprehensive battery of social and communicative assessments at each time point.

Results: In Experiment 1, preliminary analyses from a subsample showed that NR infants exhibited a negative deflection in ERPs over right occipitotemporal scalp between 200-300 milliseconds that distinguished biological motion from scrambled motion at 12 months ($p=0.019$) but not at 6 months ($p=0.132$). Conversely, differentiation was not observed in HR infants at either 6 ($p=0.206$) or 12 months ($p=0.870$).

Likewise, a significant difference in evoked mu suppression between scrambled and biological motion was detected in NR [$t=-2.17$, $p=0.038$] but not in HR infants [$t=0.47$, $p=0.65$]. In Experiment 2, preliminary analyses from a subsample indicated audio-visual integration between 78 and 198 ms over fronto-central scalp in both the HR group and the NR group; however, HR infants showed a shorter latency for bimodal components than NR infants (105.6 ms for HR versus 133.3 ms for NR).

Conclusions: Compared to NR infants, HR infants showed attenuated responses to biological motion on multiple, convergent electrophysiological markers. In contrast, HR infants showed intact multi-sensory integration, with more efficient detection of AVS compared to NR infants. The current study demonstrates, for the first time, a neural dissociation between perception of social and non-social information in infants at elevated risk for ASD.

136.013 13 Atypical Face Processing in Children with Tuberos Sclerosis Complex. S. S. Jeste^{*1}, V. Vogel-Farley², A. Norona¹, M. Gregas², S. P. Prabhu³, M. Sahin⁴ and C. A. Nelson⁴, (1)UCLA Center for Autism Research and Treatment, (2)Children's Hospital Boston, (3)Children's Hospital, Boston, (4)Boston Children's Hospital

Background:

Sixty percent of children with Tuberos Sclerosis Complex (TSC) are diagnosed with autism spectrum disorder (ASD). In this study, we investigated the neural correlates of face processing in children with TSC, using event related potentials (ERPs). We focused on face processing for two reasons. First, given the extensive literature on atypical face perception in ASD, face processing could serve as an important biomarker of ASD in this population. Secondly, face processing represents a construct that requires a combination of low-level visual processing and higher-order processing (categorization of identity), each of which could be impaired in TSC given the aberrant structural connectivity in visual projections shown in the TSC mouse model.

Objectives:

Our goal was to characterize face processing in children with TSC. Our guiding hypothesis was that children with TSC would show impairments in neural markers of early visual processing and in face perception, and that these differences would be more prominent in children with TSC/ASD.

Methods:

We studied 19 children with TSC under age 4 and 20 age matched controls using an ERP paradigm of familiar-unfamiliar faces. Six children with TSC (32%) had ASD. Components of interest included the temporal-occipital P1 (early visual processing), N290 and P400 (face processing). A repeated measures analysis of variance of hemisphere (right, left), condition (mother, stranger) and group was performed with both amplitude and latency as dependent variables. Several different groups were analyzed: (1) Controls; (2) TSC; (3) TSC/ASD; (4) TSC/no ASD; (5) TSC with temporal lobe tubers; (6) TSC with occipital lobe tubers.

Results:

Despite extensive cortical pathology, children with TSC showed robust ERP evidence of face processing. There was a main effect of diagnostic group for the N290 latency, with the TSC group showing a longer N290 latency than controls (276 msec vs. 259 msec; $p=0.05$). There was also a region by group interaction ($F=3.63$, $p=0.04$), with the TSC group failing to show the expected hemispheric differences in face processing. Post-hoc analysis showed that this interaction was driven by two factors. First, there was a significant difference for N290 latency between TSC and controls in the right hemisphere [$t(33.2)=2.68$, $p=0.01$]. Secondly, the control group showed an expected significant hemispheric difference for the N290, with N290 latency longer on the left compared to the right [$t(19)=2.98$; $p=0.008$]. The TSC group did not demonstrate this hemispheric difference. On subgroup analysis, the longest N290 latency was seen in (1) children with ASD/TSC and (2) children with temporal lobe tubers, regardless of ASD diagnosis.

Conclusions:

This is the first study to investigate face processing in children with TSC. These promising results demonstrate that children with TSC are slower to process faces, and that they lack the hemispheric specialization for face processing seen in typically developing children. We also characterize a trend towards slower face processing in children with TSC and ASD. Through this work, we have begun to define an electrophysiological biomarker of a perceptual domain critical for normative social development, with the ultimate goal of defining functional pathways to ASD in TSC.

136.014 14 Electroencephalographic Abnormalities and Epilepsy in Patients with Autism Spectrum Disorders. E. Barredo^{*1}, M. C. Miranda², M. Vazquez², C. Tomatis², P. Castro² and M. Parellada³, (1)*Hospital Gregorio Marañón de Madrid*, (2)*Hospital General Universitario Gregorio Marañón*, (3)*Child and Adolescent Psychiatry Department, CIBERSAM, Instituto de Investigación Sanitaria Gregorio Marañón, IISGM, Hospital General Universitario Gregorio Marañón*

Background: The prevalence of epilepsy and epileptiform electroencephalographic abnormalities is higher in individuals with ASD than in the general population, but the current understanding of the association between them is still unclear.

Objectives: The aims of this study were to describe the prevalence of epilepsy and epileptiform EEG abnormalities in our group of ASD patients, to identify possible risk factors associated to the development of epilepsy in these patients, and to describe their management.

Methods: Two hundred patients diagnosed with ASD according to Diagnostic and Statistical manual of Mental Disorders of the American Psychiatric Association 4th edition (DSM IV) criteria in Hospital General Universitario Gregorio Marañón, from April 2010 to February 2011 were enrolled in this study. A retrospective chart review was done. Epidemiologic data was collected as well as data on past medical history, family medical history, neurodevelopment, neurological examination, presence or absence of seizures or epilepsy and the treatment given in each case, neuropsychologic evaluation, and EEG reports including sleep and wakefulness periods.

Results: The mean age of the group subjects was 7 years (range 17 month–16 years), 82% of the

sample were male. Epilepsy was found in 14,5% of the subjects. The mean age at epilepsy onset was 48 months. Wakefulness EEG trace records were obtained in 181 patients (90%), abnormalities were found in 37 of them (18.5 %), most of them epileptiform discharges.

89% of the sample had idiopathic ASD and 11% had secondary ASD. Among the patients with idiopathic ASD 11,3% showed epilepsy. This percentage increased in patients with syndromic autism (40,9%).

52% of the sample showed different degrees of mental retardation (MR).

Epilepsy was more frequent in patients with mental retardation (15%) than in patients without mental retardation (12.5%), though this difference was not statistically significant ($p=0.106$). EEG abnormalities were found in 21.6% of patients with MR and in 17.7% without MR. There was no significant association between EEG abnormalities and mental functioning ($p=0,565$)

A history of language regression was reported in 31% of the patients, at a mean age of 18 months. Epilepsy was similar in patients with autistic regression (14%) as in non-regression patients (14.5%) ($p=1,000$).

16% of patients in the sample received treatment with antiepileptic drugs (AEDs). Of those who received treatment for the associated epilepsy, 66% did so as monotherapy and 33% in combination. The most commonly used AED was valproic acid alone.

Conclusions: The prevalence of epilepsy and EEG abnormalities observed in our sample

is at the lower limit of ranges reported in the literature, probably due to the characteristics of our sample, which had high percentage of idiopathic ASD. The prevalence is higher in patients with MR, syndromic autism and in females, the latter two reaching a statistically significant association. We conclude from our study that epilepsy is a comorbid factor of ASD and is not related to its pathogenesis.

136.015 15 Is There an Overlap Between Autism and Schizophrenia:

The Search for Shared Endophenotypes with Focus On Sensorimotor Gating. G. F. Madsen*¹, N. Bilenberg², C. Cantio² and B. Oranje³, (1)*Child and Adolescent Psychiatry, University of Southern Denmark*, (2)*University of Southern Denmark*, (3)*Center for Neuropsychiatric Schizophrenia Research (CNSR) and Center for Clinical Intervention and Neuropsychiatric Schizophrenia Research (CINS), Copenhagen University Hospital, Psychiatric Center Glostrup*

Background:

The relation between Autism Spectrum Disorders (ASD) and Schizophrenia is a matter of intense debate and research, considering evidence of common neurobiological pathways in both disorders. A growing number of systematic studies on ASD report co-occurring psychiatric symptoms and disorders to be common in these patients, and from follow up studies we know that a significant number of patients within years after diagnosis develop psychosis or even schizophrenia. The diagnostic boundaries of autism and schizophrenia have moved outward over the years and similar to autism some authors also describe "a schizophrenia spectrum". It seems to be that especially the broader phenotypes of these spectra may overlap. A large amount of literature reports on schizophrenic patient's inability to discriminate relevant from irrelevant sensory information, a phenomenon termed "sensory filtering" (or sensory gating). Similarly, individuals with autism often demonstrate abnormal reactivity to sensory stimuli, a phenomenon that is pervasively present throughout life. One of the paradigms thought to reflect filtering of sensory information is the prepulse inhibition of the startle reflex (PPI), a psychophysiological paradigm which is believed to assess so called sensorimotor gating.

Objectives:

The aims of this study were to investigate whether schizophrenia-like deficits in sensorimotor gating, habituation and sensitization of the acoustic startle reflex are present in a group of children with ASD by comparing them with a group of matched neurotypically developed controls. An additional aim was to explore possible psychophysiological subgroups within our ASD population.

Methods:

In a case-control design 35 ASD children, 8-12 years old, diagnosed according to DSM-IV-TR criteria and 40 matched NTD controls were tested with a psychophysiological tests battery. Parents to all participants completed the Social Communication Questionnaire (SCQ), Social Responsiveness Scale (SRS) and the Child Behaviour Checklist (CBCL).

Results:

PPI of the acoustic startle reflex was analyzed in 18 ASD cases and 34 NTD controls. Habituation and sensitization was analyzed in 23 ASD cases and 39 NTD controls. Patients with ASD did not display the usual drop in percentage PPI in trials with less intense prestimuli (76dB/120ms) as normally found in healthy controls. In addition, ASD cases showed significantly increased sensitization compared to controls.

Conclusions:

Combined, our results may reflect the hypersensitivity of children with ASD to sensory information. The relation to PPI deficits as observed in schizophrenia is not apparent, although it cannot be excluded that a constantly hypersensitive filter in some ASD children might eventually collapse, resulting in sensory overload of higher brain processes as currently widely believed to be the case in schizophrenia patients. Future research should therefore study the developmental course of PPI deficits in ASD patients in a longitudinal design.

136.016 16 Comparative Study of Executive Function in Three Groups of Patients: Autism Spectrum Disorder, Attention Deficit Disorder and Hyperactivity and Autistic Spectrum Disorder with ADHD Symptoms. L. Fernandez*, *Sant Joan de Déu Hospital*

Background: We have linked various childhood psychiatric disorders with executive dysfunction. The motivation for this study is the presence of impaired executive function in Attention Deficit and Hyperactivity Disorder (ADHD) and Autism Spectrum Disorder (ASD). In the current literature there are studies that show data on the comorbidity between both disorders. ADHD appears as the most prevalent disorder in children

diagnosed with ASD. Recent studies suggest that ADHD has a prevalence of 31% in ASD children.

Objectives: To study executive functions in three different groups of patients: patients with ASD without ADHD symptoms, ADHD patients and ASD patients with symptoms of ADHD. A secondary aim is to study if there are significant differences in socio-demographic variables.

Methods: A comparative cross study was carried out with three groups: ASD, ADHD and ASD + ADHD. A sample of 33 subjects of both sexes with aged between 7 and 18 was used. We used Semi-structured Diagnostic Interview (ADI-R, K-SADS) and questionnaires (Conners) for assessment of symptoms and hetero-applied questionnaires to assess executive function (BRIEF) and intellectual ability (WISC-IV/WISC-R).

Results: We applied non-parametric tests (Kruskal-Wallis and U-Mann Whitney) and we found two dependent variables which are differentially distributed and statistically significant in the different groups of patients: Working Memory and Planning. ASD Children with ADHD symptoms presented higher deficits in Working Memory, followed by ADHD. ASD patients are the subjects of the sample less affected in this variable. ASD with ADHD symptomatology group presented the worst performances in tasks of planning, followed by ADHD group. We decided to dichotomize variables. Scale scores greater than $t=65$ were considered clinically significant. Planning was the scale statistically significant.

Conclusions: Executive function (EF) appears affected in most of the sample used especially in the comorbid group. It is important take account of this deficit performance in clinical practice in the face of the EF assessment and treatment.

136.017 17 Resting State Quantitative EEG Differences At 3 Years of Age by Risk Status and Diagnostic Outcome for Autism Spectrum Disorders. A. R. Levin^{*1}, V. Vogel-Farley², H. Tager-Flusberg³ and C. A. Nelson¹, (1)*Boston Children's Hospital*, (2)*Children's Hospital Boston*, (3)*Boston University*

Background: Identification of early and predictive biomarkers for autism spectrum disorders (ASD) is of key importance, as it allows diagnosis and thus treatment to begin as early as possible, potentially resulting in improved outcomes. EEG

is one promising biomarker, as an often cited hypothesis is that autism is associated with alterations in the makeup of neural networks, with long-range underconnectivity and local overconnectivity (Geschwind & Levitt 2007), and one can infer brain-based connectivity using patterns of electrical activity. Several studies (e.g. Murias et al. 2007) have previously demonstrated altered quantitative EEG patterns in older children and adults with ASD compared to controls. In younger children, prior studies have demonstrated altered quantitative EEG patterns (Tierney et al. 2012; Bosl et al. 2011) and altered white matter fiber tract organization (Wolff et al. 2012) in children at high risk for ASD (HRA) by virtue of having a sibling with ASD, which increases the risk of developing ASD nearly 20-fold (Ozonoff et al. 2011), compared to siblings of typically developing children (low risk controls, LRC). Because neural networks change with age, further evaluation of the developmental trajectory of EEG findings in very young children at risk for ASD, and those who ultimately receive a diagnosis, is necessary in order to determine an EEG-based predictive biomarker for ASD.

Objectives: As part of a longitudinal study tracking the development of HRA and LRC children, we evaluated resting-state EEG in 3 year olds at high and low risk for ASD, and who do and do not meet diagnostic criteria for ASD, to evaluate for differences in quantitative EEG findings between these groups.

Methods: EEG was collected from children at 36 months of age with a 128 HydroCel Sensor Net System (EGI, Inc, Eugene OR) while they were seated on their mother's lap, watching a lab assistant blowing bubbles. The diagnosis of ASD was based on an ADOS by a certified examiner at 36 months of age, and confirmed by clinical impression.

Results: Preliminary analyses demonstrate that HRA children who were diagnosed with ASD at 36 months have a right frontal asymmetry in absolute high alpha power (9-13 Hz), meaning there is higher high alpha power on the right compared to the left; typically developing (TD) children from both the HRA and LRC groups have a left frontal asymmetry in this frequency band. Consistent with these differences in asymmetry, recent studies in our lab have suggested that HRA

children show an initial left frontal asymmetry at 6 months that shifts rightward by 18 months, while LRC children show right frontal asymmetry that shifts leftward over the same age range. Additionally, preliminary analyses have demonstrated that many of the spectral differences between the HRA and LRC groups seen in younger children have disappeared by age 3.

Conclusions: These findings suggest that altered quantitative EEG findings have the potential to become a biomarker for autism risk. However, between-group differences appear to change significantly over time, highlighting the importance of evaluating specific findings over the course of development.

136.018 18 Relative Contribution of Autistic Traits Versus Alexithymic Traits in the Neural Processing of Social Information. A. Desai^{*1}, A. Naples¹, M. Coffman¹, C. E. Mukerji¹, R. Tillman¹, A. Kresse², R. Bernier² and J. C. McPartland¹, (1)*Yale Child Study Center*, (2)*University of Washington*

Background:

Multiple studies indicate atypical face processing in autism spectrum disorder (ASD), but these difficulties are not universal and are subject to individual variability. This as-yet unexplained heterogeneity could be accounted for by introduction of subgroups within the diverse category of individuals presenting with ASD. One potential grouping factor is alexithymia, a disorder characterized by difficulties in the recognition and identification of emotion. Recent research demonstrates that emotion recognition impairments in ASD are predicted by its comorbidity with alexithymia (Bird et al., 2010). No research to-date has examined the relative influence of autistic and alexithymic traits on social perception in terms of brain-behavior relationships.

Objectives:

To examine the relative influence of alexithymic and autistic traits on neural circuits subserving face and action perception and associated behavior.

Methods:

Participants consisted of 28 typically developing (TD) adults screened for levels of autistic traits (using the Autism Quotient) and alexithymia (using the Toronto Alexithymia Questionnaire and the Bermond-Vorst Alexithymia Questionnaire). Behavioral measures were administered to assess social behavior (Social Responsiveness Scale), face recognition (Benton Facial Recognition Test), and theory of mind (Reading the Mind in the Eyes Test). EEG was recorded with a Hydrocel Geodesic Sensor net while participants viewed static and dynamic faces presented in three conditions encompassing both affective and neutral content (fearful, puffed cheeks, biologically impossible movement). Event related potentials (ERPs) were extracted to initial static faces, indexing basic visual processing (P100), face structural encoding (N170) and emotional arousal (late positive potential; LPP). Evoked oscillatory activity was calculated during dynamic movement of faces, indicating activity in the action-perception system (μ desynchronization).

Results:

Level of autistic traits predicted P1 amplitude and μ suppression, such that higher levels of autistic traits correlated with reduced P1 amplitude ($p=0.043$) and μ suppression ($p=0.025$). Additionally, P1 amplitude was found to predict N170 amplitude ($p=0.005$). A repeated-measures analysis of variance revealed a main effect of emotion on the μ rhythm attenuation ($F=3.86$, $p<.05$), such that fear expressions elicited reduced μ suppression compared to puffed or impossible expressions. Analyses in progress examine relationships among behavioral measures and ERP/EEG markers of social perception at each stage of processing. Preliminary regression analysis indicates unique contributions of alexithymic traits in influencing P1 and N170 amplitude and latency and μ attenuation.

Conclusions:

Results reveal distinct contributions of the level of autistic traits and alexithymia at different stages of the face perceptual process, spanning from basic visual perception to mirror neuron system activation. Understanding the relationship between ASD and alexithymia has important implications for parsing heterogeneity in autism

and applying individually tailored intervention techniques.

136.019 19 How Do Children with Autism Spectrum Disorders Solve False Belief Tasks? Insights from an EEG Study. A. S. Li*, M. A. Sabbagh and E. A. Kelley, *Queen's University*

Background: Individuals with autism spectrum disorders (ASD) have been said to have a 'deficit in theory of mind'; that is, they have difficulty reasoning about mental states and typically do poorly on false belief tasks. However, some studies have found that a proportion of children with ASD do succeed on false belief tasks (e.g., Happé, 1994). Researchers have suggested that these individuals may have arrived at the correct answers through cognitive processes that are different from those used by typically developing children (e.g., Frith, Morton, & Leslie, 1991; Happé, 1995). What exactly are these processes? Measuring electroencephalogram (EEG) alpha activity—a reliable measure of children's neurocognitive development (Thatcher, 1992)—and false belief understanding in children with ASD may provide insights into how they succeed on these tasks. Sabbagh, Bowman, Evraire, and Ito (2009) found that individual differences in EEG alpha activity localized to the dorsomedial prefrontal cortex and right temporal-parietal juncture were positively associated with performance on theory of mind tasks in typically developing children. Thus, if children with ASD succeed on false belief tasks by using theory of mind, we expect task performance to be associated with maturation of the dorsomedial prefrontal cortex and right temporal-parietal juncture. However, if children with ASD succeed on false belief tasks by following behavioural rules, we expect task performance to be associated with maturation of areas implicated in executive functioning (e.g., medial frontal regions).

Objectives: To investigate the processes by which children with ASD solve false belief tasks.

Methods: Participants are school-age boys with and without ASD matched using the Peabody Picture Vocabulary Test—Fourth Edition (Dunn & Dunn, 2007). Data collection is ongoing—we have full datasets from 15 children with ASD thus far.

Brain activity. Resting EEG alpha activity is measured using a 128-channel Geodesic Sensor Net while participants fixate on a still picture.

Theory of mind. Theory of mind is assessed using two false belief tasks: contents change (Gopnik & Astington, 1988) and location change (Wimmer & Perner, 1983).

Executive functioning. It is important to statistically control for executive functioning as performance on response-conflict executive functioning tasks seems to be associated with theory of mind development (Perner et al., 2002). The executive functioning battery includes the grass-snow stroop (Carlson & Moses, 2001), bear-dragon (Reed et al., 1984), dimensional-change card sort (Zelazo, 2006), and less is more (Carlson et al., 2005) tasks.

Results: Preliminary results are based on 12 high-functioning boys with ASD. Performance on false belief tasks was significantly related to EEG alpha activity localized to the cingulate cortex, precentral gyrus, and precuneus. Furthermore, the executive functioning battery was associated with false belief tasks, $r(10) = .713, p < .01$.

Conclusions: Development of areas typically related to executive functioning in typically developing children appear to play an important role in false belief task performance in children with ASD. Our preliminary findings support the hypothesis that children with ASD differ from typically developing children in the way they solve false belief tasks (i.e., rule-following rather than intuitive understanding).

136.020 20 Neural Correlates of Emotion Word Processing in Autism Spectrum Disorders. A. Lartseva^{*1}, T. Dijkstra² and J. K. Buitelaar³, (1)Radboud University Nijmegen Medical Centre, Donders Institute for Brain, Cognition and Behaviour, (2)Radboud University Nijmegen, (3)Radboud University Nijmegen Medical Centre, Donders Institute for Brain, Cognition and Behavior

Background: Emotion words are a special category of words. They are remembered better, automatically attract attention, and activate a network of brain regions including the limbic system, producing a different pattern in the brain activation and in event-related potentials (ERPs). One of such emotion-specific ERP components is the Late Positive Component (LPC): a long-lasting positive-going wave most prominent over centroparietal regions. For Autism Spectrum disorders (ASD), understanding emotions in others and conveying their own emotional state may be problematic. However, little is known

about neural mechanisms of emotion processing of ASD. Furthermore, most of research has been done on recognizing emotions in faces, but less is known about processing of emotion in other types of stimuli, such as language.

Objectives: To investigate processing of neutral and emotion words in individuals with ASD by using reaction times (RTs) and EEG.

Methods: We tested 21 ASD and 20 healthy controls. Participants performed a lexical decision task while their EEG and RTs were recorded. We analyzed the effects of lexicality (words vs nonwords), frequency (high vs low frequency words), and valence (positive vs neutral vs negative words).

Results: In the RT analysis, we found that both ASD and control groups provided faster responses for emotion words compared to neutral. This effect was modulated by verbal IQ scores in the ASD group but not in the control group: in patients with higher scores, the difference in RT between emotional and neutral words was much smaller. In the EEG data, lexicality and frequency had a significant effect on the ERP with similar timing and distribution in both groups. With regard to emotional valence, there was a significant group by valence interaction in the negative vs neutral valence comparison: the effect identified as the LPC was present in the control group, but not in the ASD. For the positive vs neutral valence contrast, the interaction did not reach significance, even though within-group comparisons demonstrated presence of a significant LPC effect in the control group and absence of an effect in the ASD group.

Conclusions: Even simple emotional stimuli like single words are processed differently in ASD patients. The processing of emotion is modulated by verbal IQ, and patients with high and low IQ may in fact constitute two different subtypes of ASD. The EEG data suggest that the neural mechanisms of emotion processing are different in ASD and controls. In the control group the LPC was significantly modulated by valence, with timing and distribution being consistent with other studies. The LPC is hypothesized to reflect allocation of additional cognitive resources towards emotional words, because of their greater salience and motivational importance. Because

this effect was absent in the ASD group, we surmise that in individuals with ASD emotion words are in general less salient.

136.021 21 The Effect of Oxytocin On Sympathetic Responses While Listening to Emotional Sounds in Autism. I. F. Lin^{*1}, M. Kashino¹, H. Ohta², T. Yamada², H. Watanabe², C. Kanai², M. Tani², T. Ohno², K. Ichihashi², Y. Takayama², A. Iwanami² and N. Kato², (1)NTT Communication Science Laboratories, NTT Corp., (2)Showa University

Background:

Individuals with Autism spectrum disorders (ASDs) are characterized by social dysfunction, abnormality in speech and communication, and repetitive behaviors. Some researchers suggest the possibility that all or some of these dysfunctions might be attributed to a lack of sufficient orientation to social stimuli, and some previous studies have found that oxytocin may improve social cognition and alleviate these symptoms observed in ASDs.

Objectives:

The present study aims to investigate whether communication difficulty observed in autistic people is related to a lack of sufficient orientation toward social sounds. The present study also explored whether oxytocin could improve the orientation toward social sounds in autistic people.

Methods:

Sixteen ASD and thirteen typically developed (TD) male adults participated in this study. These two groups were matched in age and IQ. All ASD participants were diagnosed by a team of three experienced psychiatrists and one clinical psychologist. In the experiment, autonomic activities (skin conductance and photoplethysmograph on fingers) toward social and non-social sounds were monitored after ASD and TD participants inhaled oxytocin or placebo (in different sessions). All these sounds were chosen from International Affective Digital Sounds, and their presentation order was pseudo-randomized.

Results:

Four-way ANOVAs were used to analyze the effect of oxytocin in individual groups of participants when they heard social, non-social, pleasant, and unpleasant sounds. Compared to TD participants, ASD participants had less sympathetic activities when they inhaled the placebo, but there was no such difference when they inhaled oxytocin. After inhaling oxytocin, all participants tended to have higher sympathetic tones for social sounds than for non-social sounds. The Pearson correlation analysis confirmed that this increase of response toward social sounds compared to non-social sounds was negatively correlated with their social skills in the ASD group.

Conclusions:

This is the first study to investigate the effect of oxytocin on sympathetic responses to emotional sounds in autism. Our findings suggest that oxytocin inhalation increases orientation responses toward social sounds in autistic people.

136.022 22 ERPs Reveal Atypical Neural Response During Empathy for Physical and Social Pain in ASD. C. Mukerji^{*1}, A. Naples¹, R. Bernier², R. Tillman¹, D. Perszyk³ and J. C. McPartland¹, (1)Yale Child Study Center, (2)University of Washington, (3)Northwestern University

Background: Empathy is a fundamental social ability affected in autism spectrum disorder (ASD). Study of motor-evoked potentials has suggested reduced embodied empathy during physical pain observation in ASD. Neuroimaging studies in typical development (TD) have indicated that empathy for social pain recruits both distinct mentalizing networks and emotion-encoding regions involved in empathy for physical pain. Our work in TD revealed that autistic traits modulated event-related potential (ERP) markers of empathic processing for both physical and social pain: a rapid negative peak (N110) and a later positive deflection (P3) associated with affective sharing and cognitive evaluation, respectively. Despite its relevance to social function, neural empathic response to social pain in ASD remains unexplored.

Objectives: This study employed ERPs to (a) contrast temporal dynamics of empathy for physical and social pain in adults with ASD and TD and (b) explore relationships among neural responses to observed social pain, empathic traits, and social function in ASD. We predicted ERPs

would reveal atypical affective response to both physical and social pain at the N110 and slower cognitive appraisal of social pain at the P3 in ASD. Social function and trait empathy were hypothesized to correlate with enhanced neural response to social pain in ASD.

Methods: Participants included 20 adult males with ASD and 20 age- and sex-matched TD controls. Empathic traits and social function were measured using the Empathy Quotient (EQ) and Social Responsiveness Scale (Adult Self-Report; SRS-A-SR). EEG was recorded with a 128-electrode Hydrocel Geodesic Sensor net while participants viewed dynamic and static stimuli displaying hands in physically painful, socially painful, or painless contexts. Participants performed an empathic task (rate distress) or a distractor task (count bracelets). ERPs were extracted for each condition at central leads (C3/C4).

Results: Preliminary results from a subsample (TD: N=14; ASD: N=7) revealed (a) enhanced N110 amplitude to painful actions in ASD ($p=.004$) but not in TD ($p=.766$) and (b) delayed P3 peak latency for social actions in the right hemisphere in ASD ($p=.018$) but not in TD ($p=.207$). In addition, social impairment in ASD correlated with N110 amplitude differentiation between observed physical and social pain ($r=-.801$, $p=.030$) during the rating task, such that higher social function was associated with enhanced response to social relative to non-social pain. Empathic traits in the subsample correlated with P3 amplitude differentiation between observed physical and social pain ($r=-.503$, $p=.020$), such that higher trait empathy was associated with greater amplitude to social relative to non-social pain.

Conclusions: ERPs revealed disruption of neural mechanisms for regulating affective response to observed pain and a specific delay in neural processing of actions during cognitive empathy in ASD. Empathy was associated with greater salience of social pain during cognitive appraisal across diagnostic categories, affirming the specific importance of neural response to observed social pain to empathic function. Lastly, enhanced salience of social relative to physical pain at the affective stage of processing was associated with overall social function in ASD, indicating

emotional sharing as a critical target for intervention and research in this population.

Clinical Phenotype Program

137 Broader Autism Phenotype

Moderator: L. Zwaigenbaum University of Alberta

This poster session highlights research concerned with the characteristics of autism traits in relatives of individuals with autism spectrum disorders. The abstracts offer perspectives on behaviour, cognition and outcomes.

137.023 23 Single-Unit Responses to Emotional Stimuli in the Human Amygdala. O. Tudusciuc*¹, U. Rutishauser², S. Wang¹, A. Mamelak³, I. Ross⁴ and R. Adolphs¹, (1)*Caltech*, (2)*California Institute of Technology*, (3)*Cedars-Sinai Medical Center*, (4)*Huntington Memorial Hospital*

Background:

Social difficulties in autism are hypothesized to result, in part, from impaired face processing and social context integration. Similar functional impairments are also apparent in amygdala lesion patients. Converging evidence thus suggests that the amygdala plays an important role in processing the socially relevant information that might be disrupted in autism. How the amygdala neurons respond to faces, or other social stimuli, and how these responses might differ in people with autism, is poorly understood.

Objectives:

Having a rare opportunity to obtain intracranial recordings from patients with intractable epilepsy, we have designed an extensive battery of behavioral paradigms to address several questions related to the role of the amygdala in processing social stimuli, precisely aimed at identifying putative disparities in the activity elicited by social stimuli in autism. Given the high co-morbidity of autism and epilepsy, up to 20% of our patients are diagnosed with autism, offering a unique opportunity to record single unit activity in the amygdala of patients with autism.

Methods:

We record single neuron activity while the participants are viewing images from four relevant categories, selected based on results from studies on restricted interests in autism: a high-autism interest category (clocks, trains, cars); a low-

autism interest category (furniture, clothes); a social category (people); and a specific interest category (reported by the participant). We compare activity in the amygdala neurons in response to social versus non-social stimuli, as well as in response to stimuli of interest to the participant versus non-interesting ones.

To investigate the sensitivity of amygdala neurons to emotional faces and parts of faces we are presenting partially masked emotional faces in an emotion discrimination task. This approach is optimal for an unbiased sampling of the face in an emotion judgment, and we are simultaneously acquiring eye-tracking data to confirm the areas in the face that are fixated by the eyes.

In addition, we investigate putative amygdala activity modulation in response to the direction of gaze in photographs of faces, in computer-generated faces, and in a real person.

We assess the role of the amygdala in social context integration by presenting bi-stable emotional faces in an emotion discrimination task in which we manipulate the perceived social context of each image with a short preceding text.

Results:

Preliminary results show that there are strong and reliable responses in the amygdala to a variety of emotional stimuli, including faces, parts of faces, and emotional scenes. We are in the process of obtaining a fuller inventory in a larger sample of participants. So far, we have indications that responses to parts of faces differ significantly among patients who have a diagnosis of autism, versus those who do not. Eye-tracking studies confirm that these differences cannot be attributed to differential eye movements, but instead are likely to arise from central processing of the stimuli.

Conclusions:

There are single neurons in the amygdala responding to a variety of social stimuli, suggesting that this brain region plays a pivotal role in extracting emotion information from faces, possibly differently in autism.

137.024 24 The Factor Structure of Cognitive and Emotional Empathy in Individuals with Autism, Their Parents and General Population Controls. R. Grove*¹, A. Baillie¹, C. Allison², S. Baron-Cohen² and R. A. Hoekstra³, (1)*Macquarie University*, (2)*University of Cambridge*, (3)*The Open University*

Background: Empathy is a vital component for social understanding as it allows an individual to make sense of and predict the behaviour of another. It is posited that some of the core features of autism spectrum conditions (ASC) can be accounted for by a deficiency in empathising, with individuals with autism and their family members scoring lower on questionnaire and cognitive tasks involving empathy. Several studies suggest that empathy is multidimensional, with at least two components: cognitive and emotional empathy. Cognitive empathy is the drive to attribute mental states to oneself and others; emotional empathy refers to the drive to respond with an appropriate emotion to another's mental state. The Empathy Quotient (EQ), a self-report measure of empathising has been studied in detail across three studies. Two studies highlighted a three dimensional structure including cognitive empathy, emotional empathy and social skills, the third showing these dimensions can be accounted for by a higher order empathy factor. However, the relationship between the behavioural subscales of the EQ and other cognitive tasks of empathy has not been assessed to date. Moreover, it is unclear whether the structure is similar across general population and clinical samples.

Objectives: The current project examined empathy using both behavioural and cognitive task data from measures including the 'Reading the Mind in the Eyes' Test and the Karolinska Directed Emotional Faces Task; tasks assessing the ability to identify emotion in another individual. The research aimed to assess whether the factor structure of empathy differs across samples stratified by genetic vulnerability.

Methods: Factor analyses were conducted to assess the latent structure of empathy across samples with a high (individuals on the spectrum), medium (first-degree relatives) or low (general population controls) estimated genetic vulnerability to autism.

Results: Analysis of the EQ highlighted a three factor model, confirming a cognitive empathy, emotional empathy and social skills factor across all the three groups. Conversely, the cognitive tasks did not primarily load on cognitive empathy, but were nearly equally related to each behavioural empathy subfactor across each group. However, the cognitive tasks were more related to emotional empathy in parents and individuals with autism compared with controls.

Conclusions: This study provides insights into the latent structure of empathy in individuals with high, medium and low genetic risk for autism. Results highlight that empathy as a behavioural trait shows evidence of multidimensionality, in which three factors can be distinguished irrespective of genetic vulnerability. However, performance measures of tasks assessing empathy were related in almost equal magnitude to all three components, rather than solely to cognitive empathy. These tasks may be more strongly related to emotional empathy in individuals with a medium to high genetic vulnerability to autism. Impairments on these cognitive tasks are likely to have wider implications on the behavioural level for emotional empathy and social skills.

137.025 25 Parenting Behaviour Among Parents of Toddlers with Autism Spectrum Disorder. G. Lambrechts^{*1}, J. P. W. Maljaars², K. Van Leeuwen², B. Maes¹ and I. Noens², (1)*Parenting and Special Education Research Unit, University of Leuven (KU Leuven)*, (2)*University of Leuven (KU Leuven)*

Background: Fortunately, theories about the causes of autism spectrum disorder (ASD) have progressed from a psychogenic explanation to a more detailed understanding of the neurobiological basis of the disorder. However, the consequence of this evolution was that parenting behaviour among parents of children with ASD remained out of the picture and has never been properly investigated, notwithstanding the specific challenges that parents of children with ASD encounter in raising their children.

Objectives: This study's main goal is to investigate parenting behaviour among parents of toddlers with ASD using two different measures. Firstly, we want to examine the structure and internal consistency of two questionnaires to measure parenting behaviour: the Parental

Behaviour Scale – short version for toddlers (PBS; Van Leeuwen, Rousseau, Hoppenbrouwers, Wiersema, & Desoete, 2011) and a new scale to measure parenting behaviours potentially more specifically relevant to toddlers with ASD. We also want to compare general and more specific parenting behaviour among parents of toddlers with and without ASD (Study 1). Secondly, we want to gain insight into parenting behaviour by means of observations (Study 2).

Methods: For Study 1, the experimental group consisted of 41 mothers or fathers of a child with ASD between two and six years old. The control group consisted of 199 mothers or fathers of a typically developing child between two and six years old. For Study 2, the data collection in the experimental group is ongoing. The control group consists of 46 mothers of a typically developing child between two and five years old. We studied parenting behaviour in the home situation and made use of unstructured and structured play tasks. The coding system exists out of seven general parenting dimensions and four scales to measure maternal autonomy support.

Results: Preliminary results of Study 1, based on the provisional scales of the questionnaires, showed higher mean scores for the control group for the general parenting scale 'Discipline' and for the new scale 'Stimulating the development'. For the experimental group, higher mean scores were found for the new scale 'Adapting the environment'. At the time of the conference, we will also have preliminary results of the observation study.

Conclusions: These studies are two of the first studies that investigate parenting behaviour among parents of a child with ASD by means of two different methods. A first indication was found that parents of toddlers with ASD report to adapt the environment more than the control group. Conversely, they report to stimulate the development of their child less. An important remark to make is that some items of this scale refer to skills that may be too difficult for toddlers with ASD. These studies will not only result in the development of new instruments to investigate parenting behaviour among parents with a child with ASD, but also in the development of instruments useful for the evaluation of

prevention and intervention programs regarding parenting a child with ASD.

137.026 26 Autistic Traits in Parents of Children with Autism NOT ONLY Explained by the Burden of Chronic Disorder. N. Gaddour*, N. Boussaid, S. Missaoui and L. Gaha, *University of Monastir*

Background:

In a previous study, higher figures of autistic traits in parents of affected children have been documented in comparison with parents of typically developing children. Among objections to that conclusion was possible explanation of some traits not necessarily by autistic traits but rather by anxio-depressive reactions to the chronic medical condition and disability in the child.

Objectives: Aim of this study was to compare autistic traits in parents of children with autism spectrum disorders (ASD) and in parents of children with chronic medical conditions (CMD).

Methods:

A case control study was conducted at the child psychiatry clinic of University Hospital F. Bourguiba, Monastir, Tunisia comparing a group of parents of children with ASD, diagnosed with CARS and according to DSM IV (N=119) and a control group of parents of children with non neurodevelopmental CMD (diabetes mellitus, asthma...) (N=71) Parents were assessed with the Adult Autism Spectrum Quotient (AQ) (Baron-Cohen *et al.* 2001) consisting in 50 quantitative items and 5 sub-scales (imagination, communication, local details, attention switching and socialization)

Results:

Global AQ scores were higher in parents of children with ASD (20) in comparison with parents of children with CMD (16,14). Considering AQ subscales, significant differences were found for imagination, attention to detail and attention switching, but no significant difference was found for communication and socialization.

Conclusions: These results mean that higher rates of autistic traits in parents of children with ASD are not explained by possible anxio-

depressive reactions to the fact of having a child with a chronic medical condition, but with structural inherited traits.

137.027 27 Model Invariance Across Genders in the Broad Autism Phenotype Questionnaire. N. B. Cox*¹, J. L. Wade² and R. E. Reeve², (1)*Curry School of Education at the University of Virginia*, (2)*University of Virginia*

Background:

The ever-increasing prevalence rate of Autism Spectrum Disorders (ASD) necessitates a more thorough understanding of the etiology of the disorder. ASD is considered one of the most heritable neuropsychiatric disorders; twin and family studies implicate at least moderate genetic heritability in the origin of disorder. The complexities of ASD, however, impede genetic dissection; researchers have yet to isolate specific autism susceptibility genes.

Recent research employs the concept of the Broad Autism Phenotype (BAP), which refers to a milder but similar presentation of traits associated with ASD in relatives of individuals diagnosed with the disorder. Application of the BAP facilitates the study of genetic effects in the BAP *and* ASD by allowing for larger sample sizes and isolating specific traits, rather than a cluster of traits in the full condition of ASD, to detect underlying genes. Several instruments have emerged to capture the BAP. Empirical evidence suggests that the Broad Autism Phenotype Questionnaire (BAPQ) demonstrates psychometric properties superior to the other self-report BAP measures.

Objectives:

The developers of the BAPQ report some strong evidence of reliability, through examination of internal consistency, and validity, based on high sensitivity and specificity of the instrument compared to direct clinical assessment of the BAP. The evidence of validity presented by the developers, while valuable, is not sufficient for the emerging uses of the BAPQ. The assumption of model invariance, which refers to the stability of the factor structure of an instrument across groups (e.g., genders), should be upheld in order to draw meaningful conclusions about the results of an instrument. Recent comparisons of mean

differences across gender on the BAPQ assume model invariance without explicitly testing it. The present study seeks to assess model invariance of the BAPQ across genders, as failing to do so yields serious implications for the interpretation of findings on the measure

Methods:

The study plans to use Confirmatory Factor Analysis (CFA) to assess model invariance across the groups, as it has emerged as the method of choice. CFA involves a hierarchy of logically ordered and increasingly restrictive tests of sets of model parameters to investigate the model stability of the BAPQ across genders. The study intends to test configural, metric, and structural invariance, but the hierarchy depends on the outcomes at each level of analysis. Model assessment at each level of analysis relies on model fit indices and inferential tests.

Results:

The researchers hypothesize that the three-factor structure model of the BAPQ does not vary across groups but complete invariance is not expected. This study anticipates that configural invariance will be upheld, indicating that the baseline model proposed by the developers of the BAPQ is stable across genders. The researchers expect to uphold metric invariance, yet will examine partial invariance provided any indications of noninvariance at this level. The current study does not anticipate stability across groups on structural invariance, given the inherent differences between males and females.

Conclusions:

Empirical evidence upholding model invariance across gender groups provides invaluable information on the validity of the BAPQ.

137.028 28 BAPQ As a Predictor of Child Functioning in Autism Spectrum Disorders. J. C. Bush*, C. R. Maxwell, O. Hsin and R. T. Schultz, *Children's Hospital of Philadelphia*

Background: Broad autism phenotype (BAP) is a milder expression of the social, non social and language impairments seen in Autism Spectrum Disorders (ASD). Most studies have used the BAP construct in the context of examining family

members of a proband with ASD for BAP characteristics. However, the relationship between BAP traits in parents of children with ASD and the proband's symptomatology remains poorly understood.

Objectives: This study examines this relationship by utilizing the Broader Autism Phenotype Questionnaire (BAPQ), Social Responsiveness Scale (SRS) and Social Communication Questionnaire (SCQ). We hypothesize that the parent BAPQ would be correlated with great ASD symptomatology in their child with ASD. We also predicted elevated BAP traits in parents of children with ASD compared to those of typically developing controls (TDC), as has been found in other studies.

Methods: One hundred nineteen children with ASD (109 Male) and 97 typically developing controls (70 Male) and their parents were enrolled in the study. ADI-R, ADOS, and expert clinical judgment were used to confirm ASD diagnoses in the children. Groups were matched on age (ASD: $M=10.9 \pm 3.2$; TDC: $M=11.2 \pm 3.6$; $p=0.52$) but not IQ (ASD: $M=99.7 \pm 22.2$; TDC: $M=114.140 \pm 14.4$; $p<0.001$) or sex ratio. Each parent was asked to complete a self-report BAPQ and a parent to child SRS and SCQ.

Results: Preliminary analyses indicate that both mothers and fathers of children with ASD have significantly higher rates of BAP traits compared to those of TDCs (Mothers: $p=0.002$; Fathers: $p=0.008$). Parental BAP total scores were not correlated to child IQ (Mother $r=-0.048$, $p=0.469$; Father $r=0.095$, $p=0.162$). Thirty-three of 238 (13.9%) ASD parents scored above the established BAP threshold compared to 12 of 194 (6.2%) TDC parents ($p=0.011$). ASD children has significantly higher SRS and SCQ scored compared to TDCs ($p<0.001$). Pearson correlations showed ASD father, but not mother, BAPQ total scores to be significantly correlated to child SRS scores ($r=0.298$, $p=0.001$). Conversely, only the TDC mother BAPQ totals were correlated to child SRS scores ($r=0.489$, $p<0.001$). Within ASD, BAP present fathers had children with significantly higher SRS scores than those fathers who did not meet BAP threshold ($p=0.026$). Neither group showed significant correlations with the SCQ.

Conclusions: As expected, BAP scores were greater for parents of children with ASD compared to TDC. Our results suggest that there may be different inheritance patterns among ASD and TDC families as ASD children's social functioning was strongly correlated to their fathers' BAP while TDC children's was strongly correlated to their mothers' BAP. Moreover, these findings should be considered in future phenotypic and genetic studies. The lack of association between BAPQ and SCQ may be explained by the fact that the Lifetime SCQ was administered and thus our scores did not reflect the child's current presentation as in the SRS. Elevated BAP in parents of children with ASD may be predictive of other important ASD subtype-like differences. A wider set of hypotheses examining this issue are ongoing with this rich dataset.

137.029 29 Are Atypical Face Processing and Reduced Joint Attention Characteristics of the Broader Autism Phenotype?. P. Novack*¹, K. Gillespie-Lynch², J. Lee³, R. Elias⁴, P. Escudero⁵, T. Hutman³ and S. P. Johnson³, (1)Washington University in St. Louis, (2)City University of New York, (3)University of California, Los Angeles, (4)University of California, Berkeley, (5)MARCS Institute, University of Western Sydney

Background: Autism is often characterized by atypical face processing including reduced attention to eyes and increased attention to mouths (Klin et al., 2002; Jones et al., 2008), and decreased joint attention (e.g. Sigman & Ruskin, 1999). Decreased attention to eyes was concurrently associated with more autistic symptomatology (Jones et al., 2008; but see Klin et al., 2002) but may not predict later diagnostic outcomes for infant siblings of children with autism (Young et al., 2009). Additionally, increased attention to mouths was associated with decreased social symptoms among adults with autism (Klin et al., 2002). Reduced joint attention is longitudinally associated with increased symptoms of autism (Gillespie-Lynch et al., 2012). Given that atypicalities of face processing and joint attention distinguish between individuals with and without autism and may be associated with autistic symptomatology, they could be characteristics of the broader autism phenotype (BAP). Both individuals with autism and their non-autistic siblings looked less at eyes than controls (Dalton et al., 2006). However, reduced joint attention may be specific to siblings who are

themselves diagnosed with autism (Rozga et al., 2011).

Objectives: This eye-tracking study investigates whether atypical face processing and reduced joint attention are characteristics of the BAP by determining if they a) distinguish between children with and without autism and b) are associated with symptoms of autism among non-autistic siblings of children with autism.

Methods: Participants included 20 children with and without autism matched by chronological age (mean age 56 months) and eighteen 36 month-old siblings of children with autism who did not meet criteria for autism. Participants were shown a video of a smiling model while their eye movements were tracked with a Tobii 1750 eye-tracker. After each participant fixated on an attention getter, the model looked toward the participant, turned to the left or right toward one of two identical objects, labeled it, and looked at it. The model's direction of gaze was counterbalanced across 8 trials. Symptoms of autism were assessed with the ADOS.

Results: Children with autism exhibited less joint attention ($t(38) = 3.022, p = .005$) and less attention to eyes ($U(38) = 125.5, Z = -2.015, p = .044$) than children without autism. No group differences in attention to the mouth were observed ($p = .570$). No associations between face processing or joint attention and symptoms of autism were observed among non-autistic siblings of children with autism ($p > .05$). Interestingly, attention to the mouth ($r_s(16) = .492, p = .038$) but not the eyes ($p = .265$) was associated with joint attention among siblings at 3 years of age. No such association was observed for children with or without autism at a mean age of 4.5.

Conclusions: Children with autism exhibited less joint attention and less attention to eyes than typically developing children. However, no associations between gaze patterns and autistic symptomatology were observed among non-autistic siblings of children with autism. This study does not provide evidence that atypical joint attention or atypical face processing are characteristics of the BAP.

137.030 30 The Broader Autism Phenotype in Parents of Multiplex Versus Simplex Autism. E. Sucksmith*¹, I. A. Roth¹, C. Allison², S. Baron-Cohen² and R. A. Hoekstra¹, (1)*The Open University*, (2)*University of Cambridge*

Background: Previous studies suggest that unaffected first-degree relatives of people with ASC display mild difficulties or superiorities on neuropsychological tasks compared to control groups, reflecting a milder expression of the full clinical phenotype (Baron-Cohen and Hammer, 1997; Happé et al., 2001; Losh et al., 2009; Wheelwright et al., 2010). Some of these studies have suggested that this broader cognitive phenotype is restricted to a subset of genetic relatives (Losh and Piven, 2007; Losh et al. 2009), but few have assessed whether it is restricted to the relatives of multiplex autism families. Phenotypic differences between multiplex and simplex autism parents may indicate that differential genetic mechanisms are operating in these two different kinds of families (Abrahams and Geschwind 2008; Sebat et al. 2007).

Objectives: To explore the broader cognitive phenotype of autism in multiplex vs. simplex parents and controls using a battery of neuropsychological tests assessing social cognition.

Methods: This study included 3 samples: i) 64 parents of autistic probands from multiplex autism families (32 fathers, 32 mothers); ii) 60 parents of autistic probands from simplex autism families (30 fathers, 30 mothers); and iii) 64 age and education-matched controls (32 males, 32 females). Apart from age and education, multiplex and simplex parents were also matched on verbal IQ and non-verbal IQ. Proband diagnoses were verified using the 3Di developmental, diagnostic and dimensional interview (Skuse et al. 2004) and the Autism Diagnostic Observational Schedule (Lord et al. 2000). Parents and controls were administered a modified version of the Karolinska Directed Emotional Faces Task (KDEF; Lundqvist et al. 1998) and the adult version of the 'Reading the Mind in the Eyes' Task (Baron-Cohen et al. 2001) assessing basic and complex emotion recognition respectively.

Results: Multiplex parents had significantly poorer mentalizing ability than simplex parents; they were significantly less accurate at identifying

complex mental states from the eye region of the face ($p < 0.05$), after controlling for verbal intelligence. Results on the KDEF suggested sex-specific difficulties recognising negative basic emotions in multiplex compared to simplex parents or controls, including sadness in ASC fathers ($p < 0.05$) and fear in ASC mothers ($p < 0.01$). There were no significant differences in performance between simplex parents and controls on the emotion perception tasks.

Conclusions: These results provide support for the hypothesis that differential genetic mechanisms may operate in simplex vs. multiplex autism. Emotion perception and social cognitive difficulties may represent an underlying genetic liability for ASC that aggregates in the first-degree relatives of probands from multiplex autism families.

Core Deficits Program

138 Infant Cognition and Behavior

138.031 31 Emergence of Social Deficits During the Second Year of Life in Infants with ASD. A. Dowd*, E. Prince, E. B. Gisin, S. H. Kim, S. Macari and K. Chawarska, *Yale University School of Medicine*

Background: By 24 months, children with autism spectrum disorder (ASD) have marked social deficits in initiating interactions and responding to bids for attention. These impairments and their precursors have been seen in infants as young as 12 months, with recent prospective studies showing that infants later diagnosed with ASD often have deficits in eye contact, responding to their name, showing, imitating, and engaging in play-based activities (Landa, 2007; Macari, 2012; Nadig, 2007; Rozga, 2011). However, further research is needed to explore the emergence and progression of these social deficits within the second year for infants later diagnosed with ASD, with atypical features and delays (ATYP) and typically developing children (TD).

Objectives: 1) To compare specific social deficits at 12, 18, and 24 months in infants later diagnosed with ASD, ATYP, and TD; 2) To explore when these deficits emerge as unique characteristics of ASD.

Methods: 105 infants at high ($n=64$) and low ($n=41$) risk for ASD were assessed at 12, 18, and 24 months using the ADOS-Toddler Module. Children were assigned a clinical best estimate

diagnosis of ASD (n= 18), ATYP (n=32) or TD (n=55) at 36 months. Social behaviors were quantified based on 4 ADOS items: Level of Engagement (B17), Response to Name (B7), Ignore (B8), and Showing (B12). The items were recoded into 0/1 categories with 0 denoting robust social behavior and 1 capturing any atypicalities or deficits. Chi-squared analyses identified significant group differences at each time point.

Results: Level of engagement exhibited by the toddlers with ASD was significantly limited compared to the TD toddlers at all three time points: 12 months ($p=.022$), 18 months ($p<.001$), 24 months ($p<.001$) and compared to the ATYP toddlers at 18 ($p=.027$) and 24 months ($p=.001$). The toddlers with ASD responded significantly less to their name than their ATYP ($p=.024$) and TD ($p=.002$) peers at 18 months and their TD peers at 24 months ($p=.042$). There was also a marginally significant difference at 12 months (ASD to TD: $p=.057$). The toddlers with ASD were less likely to request a bid for attention when ignored than the ATYP and TD groups at 24 months (ATYP: $p=.004$, TD: $p<.001$). Both the ASD and ATYP groups engaged in significantly less showing than the TD group at 12 months (ASD: $p=.014$, ATYP: $p=.011$). By 18 and 24 months, the toddlers with ASD showed significantly less than both the ATYP and TD groups (all significant at $p<.01$).

Conclusions: Marked deficits in level of engagement, showing and response to name uniquely characterized the ASD group at 18 months. Inconsistent patterns of group differences at 12 months reflect both heterogeneity in onset of ASD symptoms and variability in the skills of the infants in the ATYP group. By 18 months, however, toddlers with ASD presented with clear deficits in these critical social behaviors and seem to plateau developmentally, while their peers with delays experienced gains in these areas. The group differences emerging between 12 and 18 months suggest a critical period for developing important social behaviors.

138.032 32 Development of Nonverbal Communication Predicts Symptom Severity in Infants At Risk for ASD. B. E. McCarthy^{*1}, M. Del Rosario¹, M. Sigman¹, S. P. Johnson² and T. Hutman¹, (1)University of California, Los Angeles, (2)UCLA

Background: Nonverbal communication skills—including joint attention (JA) and requesting behaviors (RB)—are an essential component of early social interaction, intersubjectivity, and verbal communication. Impairments in these skills are among the earliest behavioral markers of Autism Spectrum Disorder (ASD) (Rozga et al., 2011). Atypical trajectories of joint attention skills have been reported for children diagnosed with ASD by 24 months relative to typically developing (TD) children and children displaying features of the broader autism phenotype (BAP). At 14 months, levels of initiating joint attention (IJA) differentiated infants diagnosed with ASD at the same age from those later diagnosed at 24 months (Landa, Holman, & Garrett-Mayer, 2007). These early social skills are related to social and behavioral symptoms secondary to ASD (Hutman et al., 2011), but the relation between JA development during the second year and primary symptom severity of ASD has not been evaluated.

Objectives: The current study investigated the development of nonverbal communication skills (both JA and RB) from 12 to 18 months and links with autism symptom severity in infants at high- and low-risk for ASD. We hypothesized that children who experienced slower (i.e., less improved) development in these areas in the second year would present more severe symptomatology of ASD at 36 months. This developmental relationship would have implications for early detection of ASD as well as the focus and timing of early intervention.

Methods: Infant siblings of children with autistic disorder (n=111) and infants with no familial history of ASD (n=43) were assessed at 12, 18, and 36 months of age. JA (initiations and responses) and RB were assessed using the Early Social Communication Scales (Seibert, Hogan, & Mundy, 1982). A symptom severity algorithm (Gotham et al., 2009) was applied to the Autism Diagnostic Observation Schedule at 36 months (Lord et al., 2000). Hypotheses were initially tested using bivariate Pearson correlations. Where significant relations were observed, regression models were run to evaluate baseline language skills as a covariate and as a potential mediator between nonverbal communication skills and ASD severity.

Results: Baseline measures of responsive JA (RJA) and changes in RJA from 12-18 months predicted ASD severity at 36 months (p 's < .01), even when baseline language skills were controlled. Infant-initiated JA (IJA, pointing and showing, $p = .01$) at 12 months, but not change in IJA, predicted ASD severity. RB (pointing) at 12 months and change in these requesting behaviors predicted ASD severity (p 's $\leq .01$), controlling for baseline language skills.

Conclusions: While previous research indicates that early nonverbal communication skills and rates of development affect later social skills secondary to ASD, our findings demonstrate an association between change in nonverbal communication skills (JA and RB) and subsequent ASD symptom severity. Research of this kind accentuates the importance of monitoring and treating early social communication skills in order to improve developmental outcomes in infants at risk for ASD.

138.033 33 Differences in Adaptive Socialization Skills in ASD Vs. Non-ASD Developmental Delays in the First Two Years of Life. C. A. Saulnier^{*1}, K. E. Caravella¹, A. Klin¹ and K. Chawarska², (1)Marcus Autism Center, Children's Healthcare of Atlanta & Emory University School of Medicine, (2)Yale University School of Medicine

Background:

Research shows that delays in adaptive behavior are evident in children with ASD as young as age two, and that specific adaptive skills can differentiate toddlers with and without ASD matched on developmental level (Ventola et al., 2012). Studies also suggest that a gap between cognitive and adaptive skills increases with age (Kanne et al., 2010; Klin et al., 2007). Less information is known on profiles of adaptive functioning in children prior to age two.

Objectives:

This study investigates patterns of development of adaptive socialization skills between 12 and 24 months in toddlers with ASD and non-ASD developmental delays (DD) matched on verbal and nonverbal skills.

Methods:

Participants included toddlers at both high and low risk for ASD with age-2 preliminary diagnoses in the following categories: ASD ($n=19$; 74% male) and non-ASD Developmental Delays ($n=20$; 95% male). The *Mullen Scales of Early Learning*, the *Vineland Adaptive Behavior Scales, Expanded Form*, and the *ADOS Toddler Module* were administered at 12, 18, and 24 months.

Results:

No differences in Mullen scores were observed between diagnostic groups at any age. ANOVA results revealed significant differences between groups in Vineland Interpersonal age equivalent scores at 12 [$F(1,36)=44.7$; $p<.01$] and 24 [$F(1,36)=170.8$; $p<.01$] months, and Vineland Play/Leisure scores at 12 [$F(1,36)=18.3$; $p<.05$], 18 [$F(1,36)=59.1$; $p<.01$], and 24 [$F(1,36)=12.1$; $p<.01$] months, with the ASD toddlers having lower scores at all ages. Repeated Measures ANOVA results revealed that the gap between Mullen Visual Reception and Vineland Interpersonal age equivalents significantly increased from 18 to 24 months [$F(1,30)=81.9$; $p<.001$], and that this gap was larger in the ASD (10 months difference) than the DD group (7 months difference) by 24 months of age [$F(1,35)=4.5$; $p<.05$]. Pearson Correlations showed a significant negative association between Interpersonal skills and the Restricted and Repetitive Behaviors algorithm of the ADOS-T for the ASD ($r = -.47$; $p<.05$) but not DD group. Interestingly, a positive correlation was found between Play/Leisure age equivalents and the ADOS Social Affective algorithm score for the ASD ($r = .53$; $p<.05$) but not DD group, suggesting that as social affective symptoms increase, so do play and leisure scores.

Conclusions:

Results provide profiles of adaptive socialization skills in ASD in the first two years of life, with a concerning gap between early cognitive skills and adaptive interpersonal skills emerging as early as 18 months of age. By age 2, toddlers with ASD are lagging behind developmental expectations in interpersonal skills by 10 months. Distinctions between toddlers with ASD from non-ASD developmental delays are also evident in both adaptive socialization skills and diagnostic symptomatology despite no differences observed

in developmental ability between the groups. These findings strengthen the utility of using the Vineland as part of the diagnostic differential in children at or under the age of two. Given the positive correlation between adaptive play skills and social/affective symptomatology, future studies investigating item-level differences in adaptive skills at these young ages is needed, as this could be a reflection of heightened solitary and leisure-time play behaviors often observed in ASD.

Core Deficits Program

139 Core Deficits: Language Development

139.034 34 Intonation Differences of Children with ASD or SLI. G. Kiss*, J. van Santen, E. T. Prud'hommeaux and L. M. Black, *Oregon Health & Science University*

Background:

Prosody is often atypical in Autism Spectrum Disorder (ASD), but few studies have characterized this atypicality quantitatively. Studies examining intonation (i.e. pitch variation) generally only analyze overall statistical properties of pitch values in a speech sample, such as the mean and variance; these are commonly higher in speech of children with ASD than in those with typical development (TD). However, no studies have investigated how these statistical properties relate to the shapes of pitch contours of individual utterances – the “melodies of speech” – that may be key to how we perceive intonation of individuals with ASD.

Objectives:

The purpose of this study is to analyze atypical prosody of children with ASD by inferring the shapes of pitch contours from overall statistical properties of pitch.

Methods:

The data consisted of transcripts of ADOS recordings of 111 children, ages 4-8. Participants included children with typical development (TD); ASD meeting the criteria for language impairment (ALI); ASD without language impairment (ALN); and specific language impairment (SLI). An iterative algorithm created four pairs of groups matched on specific measures: TD (25) vs. ASD

(23), matched on chronological age (CA) and nonverbal IQ (NVIQ); ALN (18) vs. TD (19), matched on CA, NVIQ, and verbal IQ (VIQ); ALI (18) vs. SLI (17), matched on CA, NVIQ and VIQ; and ALI (18) vs. ALN (20), matched on CA, the Social Communication Questionnaire, and the ADOS Severity Score.

We used the Simplified Linear Alignment Model (SLAM) of intonation to parameterize contour shape, using ten parameters: phrase start, middle, and end, as well as different levels of accents.

We created 2000 sets of SLAM parameters, randomly generating SLAM parameters from realistic ranges mimicking different speaking styles. We used the CSLU speech synthesizer to synthesize the pitch curves for 1000 sentences chosen randomly from the transcriptions of the children’s speech, for each of the 2000 parameter sets, giving 2 million pitch curves. For each parameter set, we calculated robust statistical features of the curves, such as median, inter-quartile range, etc. from all pitch values, and statistics of the per-utterance statistics. We then trained machine learning models (linear regression, support vector regression) to relate these features to the SLAM parameters, and validated the effectiveness of the models in a ten-fold cross-validation scheme.

In the second step, we calculated the same features for the ADOS recordings, and used the previously trained machine learning models to estimate the SLAM parameters for each child. Finally, we examined whether there are group differences in the SLAM parameters.

Results:

We found that the phrase start and phrase middle parameters of the TD group were significantly lower than in the other three groups, whereas the ALN, ALI, and SLI groups did not differ from each other significantly. None of the other phrase and accent curve parameters differed significantly.

Conclusions:

We conclude, first, that overall statistics can be used to draw inferences about individual pitch

contours. Second, that these groups have different pitch contour shapes. Third, that these features may not be specific to ASD.

139.035 35 Young Children with Language Difficulties: A Dimensional Approach to Subgrouping. R. M. Jansen*, E. Ceulemans, J. Grauwels, I. Zink, J. Steyaert and I. Noens, *University of Leuven (KU Leuven)*

Background: Language difficulties are among the most common developmental problems that clinicians encounter in young children (Buschmann et al., 2008). Nonetheless, the heterogeneity within this group presents challenges, both with respect to diagnostic decision making and intervention. Language difficulties are associated with several developmental disorders such as specific language impairment (SLI), intellectual disability (ID), and autism spectrum disorder (ASD) (Conti-Ramsden & Durkin, 2012). Within diagnostic frameworks as the DSM-IV-TR and ICD-10, these disorders are neatly separated by fixed sets of diagnostic criteria. Especially in young children, however, behavioural overlap between children with a different clinical diagnosis has been reported as well as variability between children categorized into the same diagnostic entity. These findings suggest that the currently demarcated, often top-down constructed, diagnostic categories do not sufficiently capture the complex behavioural profiles of rapidly developing young children (Huziak, Achenbach, Althoff, & Pine, 2007).

Objectives: This study aims to delineate more homogeneous subgroups of young children with language difficulties. A dimensional, bottom-up approach is used for this purpose, thereby constructing clusters that are based on the abilities of children across developmental domains.

Methods: 36 children with receptive and/or expressive language difficulties were recruited prospectively and consecutively from two diagnostic centres in Leuven (Flanders, Belgium). The children (between 24 and 46 months of age) were raised in a monolingual Dutch-speaking household and included regardless of their clinical diagnosis. Although most children were involved in an extended diagnostic evaluation trajectory at the time of data analysis, some did receive a clinical diagnosis of ID ($n = 5$), ASD ($n = 5$) or ASD with co-occurring ID ($n = 3$). The cognitive,

adaptive and linguistic abilities of all children were assessed in addition to their mastery of two linguistic prerequisites; intentional communication and symbol understanding. The severity of ASD related characteristics present in each of the children was measured as well.

Results: Four subgroups of young children with language difficulties were delineated. Besides differences in cognitive abilities, clusters were distinguished by differences in symbol understanding, frequency of communication for behaviour regulation and severity of ASD related characteristics. Children with and without a clinical diagnosis were found within a single cluster as were children with a different diagnostic classification.

Conclusions: The results confirmed previous accounts of behavioural overlap in young children with a different clinical diagnosis and underscore the importance of adopting a dimensional, multidisciplinary approach to the phenotyping of young children with language difficulties. Both in clinical practice and research. The development of the majority of the participants was followed over a twelve-month time interval. Data regarding the association between cluster membership and later language development will also be presented.

139.036 36 Interrater Reliability Between Parents' and Preschool Teachers' Ratings of Language in Children with Childhood Autism. A. Nordahl Hansen*¹, A. Kaale² and S. E. Ulvund¹, (1)*University of Oslo*, (2)*Oslo University Hospital*

Background:

Children with childhood autism often fall below basal levels on standardized direct assessments for language competence (Charman et al., 2003). Several researchers thus suggest the use of report-based language assessments for young children with autism (Charman, 2004; Tager-Flusberg et al., 2009). The centrality of language development in understanding autism, and the increasing numbers of children diagnosed with the disorder early on in preschool years underline the need for reliable, valid and effective measurements (Charman et al., 2003). However, some claim that parent-reports tend to overestimate the child's abilities compared to reports from others that know the child well (Tomasello & Mervis, 1994). The accuracy of parent-report

assessments has, and still is a topic of intense debate.

Objectives:

The aim of this study was to investigate interrater-reliability between parents' and preschool teachers' ratings of language in children with autism.

Methods:

Parents and preschool teachers of 61 children with a diagnosis of childhood autism (aged 2-4 years) separately filled out the MacArthur-Bates Communicative Development Inventory; Words and Gestures (CDI - WG: Fenson et al., 2007), a widely used report-based language measure. Interrater reliability between parents' and preschool teachers' ratings was estimated for children's language production and language understanding. Pearson's *r* was used to analyze the correlations between parents' and preschool teachers' ratings. The Spearman-Brown formula was then used to estimate the interrater reliability. Although most used for split-half reliability, the Spearman-Brown formula is also applicable to interrater reliability analysis (Fan & Chen, 2000).

Results:

Mean ratings of word production were 121 for parents and 109 for preschool teachers, while mean ratings of word understanding were 182 for parents and 158 for preschool teachers. Analyses showed high correlations ($r = .93^{**}$) between parents' and preschool teachers' ratings on language production. For language understanding, preschool teachers and parents correlated lower, but still high ($r = .79^{**}$). Spearman-Brown reliability analyses showed $R = .96$ for word production, and $R = .88$ for word understanding.

Conclusions:

The high levels of interrater reliability between parents and preschool teachers obtained in this study strengthen psychometrical properties of the CDI as a reliable measure when assessing language production and -understanding in children with childhood autism. This supports

proposals from Charman (2004) and Tager-Flusberg et al. (2009) that report-based assessments should be included when testing language skills in children with autism. The results also suggest that both parents and preschool teachers are useful sources of information. Although parents tended to rate children's language skills slightly higher compared to preschool teachers, this may just as well be interpreted as contextual differences between home and preschool, as opposed to interpretations of parents' over-estimation. Based on our findings the CDI may be a valuable and cost-effective alternative to direct testing where the latter is difficult, as often is the case when testing children with autism (Charman, 2004).

Genetic Factors in ASD Program

140 Common Genetic Variants in Autism

140.037 37 A Genome Wide Association Study in Families with MORE THAN ONE CHILD with ASDs. P. Zavattari¹, L. Boccone², R. Fadda^{*1} and G. S. Doneddu³, (1)University of Cagliari, (2)ASL 8, University of Cagliari, (3)Azienda Ospedaliera Brotzu

Background: Several family studies have indicated a high heritability for autism, with evidence for a strong genetic basis. The risk of autism in siblings of autistic individuals is reported as approximately 20%, which is higher than the general population prevalence (Baird et al., 2006). However, despite such evidences of a genetic susceptibility, a number of studies failed to identify a unique allele as the basis of an high risk of Autism Spectrum Disorders. Recent studies are focusing on locus heterogeneity by which the same phenotype is caused by risk alleles at multiple different loci (Amaral, Dawson and Geschwind, 2011). Population with high level of genetic transmitted diseases (ie: type 1 diabetes), like for example people living in geographically isolated places, might be particularly interesting to study for ASDs risk, due to their peculiar genetic homogeneity.

Objectives: This study aimed to identify risk alleles in families with more than one child with ASDs in a sample of Italian families, living in an island in the south of Italy (Sardinia) with high level of genetic homogeneity, by employing a genome-wide association methodology.

Methods: For the present study we selected 8 families, each one with two children affected by idiopathic autism. We realized a genome-wide association study (GWAS) and a copy number variant (CNV) analysis by the means of whole-genome genotyping arrays HumanOmni1-Quad. Specifically, we purified genomic DNA by salting out extraction from blood samples of patients and their parents. Samples concentration was evaluated by absorbance (Nanodrop 1000) and fluorometric reading (Pico-green/Qubit). Each sample was genotyped using commercial chip, that interrogate more than a million points in the genome, including single nucleotide polymorphisms (SNPs) and copy number variants (CNVs).

Results: Our analysis revealed genomic variations at the level of recurrent CNVs. In particular, some do not seem to co-segregate with the trait of interest. On the contrary, a CNV mapping on chromosome 17q12, shows, in approximately 30% of patients analyzed, only one copy of genomic DNA. This is a region extending from 1.5 to 3.3 Mb, in the different patients. The region contains the following genes: TBC1D3B, CCL3L1, TBC1D3C, CCL3L3, CCL4L1, TBC1D3H, TBC1D3C, TBC1D3G. The TBC family of genes encodes for proteins involved in RAB GTPase signaling and vesicle trafficking; the CCL family of genes encodes for cytokines, secreted proteins involved in immunoregulatory and inflammatory.

Conclusions: These preliminary results are suggestive of interesting developments but need to be replicated in a larger sample, in which we would endeavor to confirm the results highlighted by the chip, by real-time PCR. Moreover, it might be of interest to evaluate the possible genotype correlations identified through the present study.

140.038 38 Genome-Wide Investigation of Social-Communication Traits and Their Heritability in the Avon Longitudinal Study of Parents and Children - a Longitudinal Perspective. B. St. Pourcain^{*1}, W. Mandy², J. Golding¹, S. M. Ring¹, W. L. McArdle¹, N. J. Timpson³, J. P. Kemp¹, D. M. Evans¹, D. H. Skuse⁴ and G. Davey Smith¹, (1)University of Bristol, (2)Faculty of Brain Sciences, UCL, (3)School of Social and Community Medicine, (4)Institute of Child Health, UCL

Background:

Social communication difficulties represent an autistic trait, which is heritable and persistent

during the course of development. Little is known however about variations in heritability and genetic association signals spanning childhood and adolescence.

Objectives:

Our study aimed to undertake a genome-wide investigation of social communication symptoms during childhood and adolescence using both single-time point and longitudinal approaches, and an estimation of the heritability at different developmental stages.

Methods:

We performed a genome-wide association study on mother-reported social communication problems as captured by the Social and Communication Disorders Checklist (SCDC), which 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 ≤ 5628; 2883 males, 2745 females). We selected a 2-stage analysis approach in order to facilitate a computationally efficient genome-wide screen. During the first stage, we derived single-time point estimates using a Quasi-Poisson regression framework. During the second stage, we modelled the continuous change in social communication symptoms using the best-fitting multi-level Poisson model for all single-time point SNP signals below our selection threshold ($P \leq 1E-05$). Using ranktransformed sex- and principal component adjusted social communication scores with a normal data distribution, we also conducted 'Genome-wide Complex Trait Analysis (GCTA)' in order to estimate the proportion of additive phenotypic variance explained by all SNPs (narrow-sense heritability).

Results:

Quasi-Poisson regression identified 34 independent signals ($P \leq 1E-05$) across the four investigated time-points. The strongest single-point SNP signal (rs4453791) with genome-wide evidence for association was observed near a sodium channel encoding gene (voltage-gated, type XI, alpha subunit; *SCN11A*) on chromosome 3p22.2 at the age of 17 years (beta[changes in SCDC log-scores per risk allele]=0.23; $P=9.31E-$

09). There was no evidence however that this signal contributed to association with SCDC scores at an age of 8 or 11 years ($P < 0.26$), although there was moderate evidence for association with social-communication difficulties at the age of 14 years ($\beta = 0.13$; $P = 0.0014$). Combining the effect estimates in a multilevel Poisson framework did not increase the evidence for association ($\beta = 0.085$, $P = 0.014$) although there was evidence for a SNP \times Age interaction effect ($P = 0.0013$). In parallel, GCTA revealed that the narrow-sense heritability was highest at the beginning (age 7 years, $h^2 = 0.23$, $P = 8.0E-05$) and at the end of puberty (age 17 years, $h^2 = 0.45$, $P = 3.2E-09$). Measures within mid puberty however demonstrated considerably lower heritability (age 11 years: $h^2 = 0.16$, $P = 0.0059$; age 14 years: $h^2 = 0.078$, $P = 0.12$).

Conclusions:

Our analysis revealed that neither genetic associations nor heritability estimates for parent-reported social communication difficulties may remain stable during the course of childhood and adolescence, despite the observed phenotypic stability of the most severely affected individuals observed in previous research. Our findings emphasize the presence of age-specific genetic associations and highlight the model complexities of longitudinal frameworks aiming to capture these signals. We are now undertaking analyses investigating factors contributing to the observed variation in heritability. For replication purposes we will also investigate the observed SNP signals in autism samples, such as families from the Autism Genetic Resource Exchange.

140.039 39 Norepinephrine Transporter Gene (SLC6A2) Is Quantitatively Associated with Behavioral and Cognitive Functions in Autism Spectrum Disorder. H. J. Yoo^{*1}, I. H. Cho², J. E. Park¹, S. C. Cho³, B. N. Kim⁴, J. W. Kim⁴, M. S. Shin⁴, S. Park³, S. A. Kim⁵ and M. Park⁶, (1)Seoul National University Bundang Hospital, (2)Gacheon University of Medicine and Science, (3)Seoul National University Hospital, (4)Seoul National University College of Medicine, (5)Eulji University Medical College, (6)mira@eulji.ac.kr

Background: Autism spectrum disorder (ASD) is a highly heritable condition, which is related to complex genetic mechanisms involving multiple neurotransmitter systems. The high level of anxiety and stress sensitivity in ASD suggest the possible involvement of the norepinephrine

system, but the role of this system has been little explored. An association with the norepinephrine transporter gene (SLC6A2) was mainly reported in attention deficit hyperactivity disorder, but any genetic association studies have not been reported in ASD.

Objectives: The objective of this study is evaluating relations SLC6A2 gene and behavioral and cognitive phenotypes of ASD in Korean population. In the family-based association study of ASD, significant association of SNPs in SLC6A2 gene and ASD might be expected and the specific genotype of SLC6A2 might be related to certain phenotypes of ASD, especially social anxiety, vigilance to specific sensory stimuli, stereotyped and repetitive behaviors, and executive dysfunction as well as attention problems.

Methods: All subjects were initially screened for pervasive developmental disorders by two child psychiatrists based on DSM-IV-R criteria, using Korean versions of ADOS and ADI-R. Behavioral and cognitive characteristics were assessed by Social responsiveness scale, Asperger syndrome diagnostic scale (ASDS), Aberrant behavior checklist, Leiter's international performance test, and executive functions tests. Any subjects with clinically significant neurological diseases, serious medical conditions or known chromosomal anomalies were excluded. The probands and siblings were ascertained by same protocol. Ten SNPs in SLC6A2 were selected from common tagSNPs (Minor allele frequency = 0.1, $r^2 = 0.8$) for Asian populations at the international HapMap project homepage. Genotyping was performed using genomic DNA isolated from blood samples, and SNPs were genotyped using the GoldenGateTM Assay (Illumina, San Diego, CA, USA). We checked for Mendelian inheritance errors by using the Merlin-1.1.2 software to assess data quality and detect genotypic errors; the genotypes of families with Mendelian inheritance error were reset to 0 at the time of coding. We performed the family-based candidate gene analysis using transmission disequilibrium test (TDT), DFAM and QFAM tests (PLINK v1.07) for SNPs and behavioral domains of ADOS, ADI-R, rating scales measuring behaviors of ASD and executive functions tests.

Results: Total 811 individuals (205 probands, 155 siblings, 410 parents and 41 other relatives) were recruited for analyses (mean age of

probands = 95.02±51.63, 14.0% female). (1) One SNP (rs41153) is significantly associated with ASD in trio-only analysis by TDT with recessive mode ($p < .05$). (2) There was difference in the severity of Restricted, repetitive, & stereotyped patterns of behavior measured by ADI-R according to genotypes of 3 SNPs of SLC6A2 gene (rs4783899, rs1814270, rs187714). (3) There are significant association between behavioral and SNPs of SLC6A2 gene by QFAM test, including language/behavior problems in ASDs and total performance IQ, word stroop test, response time variability in continuous performance test and color sequence errors in Children's color trail making test 2 ($p < .05$).

Conclusions: This family-based association study suggests that SLC6A2 might be involved in pathogenesis of ASD, especially in specific phenotype traits, especially on cognitive functions including performance IQ and attention.

140.040 40 Oxytocin Receptor (OXTR) Gene Polymorphism

Contributes to Ability in Face Recognition Memory. D. H. H. Skuse*¹, A. Lori², I. Lee³, J. F. Cubells⁴, E. Binder⁵, T. Lehtimäki⁶, K. Puura⁷, K. Conneely² and L. J. Young⁸, (1)*Institute of Child Health, University College London*, (2)*Emory University School of Medicine*, (3)*UCL Institute of Child Health*, (4)*Emory Autism Center*, (5)*Max Planck Institute of Psychiatry*, (6)*Tampere University and University Hospital*, (7)*Tampere University Hospital*, (8)*Emory University*

Background: The ability to visually identify individuals, accomplished by facial recognition, is essential for successful social interactions. In autism, this ability is impaired. Social recognition abilities such as face recognition memory are heritable, thus by implication are influenced by genetic polymorphisms. On the basis of animal studies, the oxytocin receptor (OXTR) gene plays a critical role in conspecific recognition memory. We hypothesized that polymorphisms in this gene could contribute to variability in social recognition in humans.

Objectives: Our aim was to investigate the association between specific OXTR variants and face recognition memory, in children with autism and their family members. We selected this sample because our previous work had shown it was enriched for face recognition memory impairment, compared with typical population controls.

Methods: 661 participants from 194 families were recruited including 198 probands with autism (mean age=11.3±3.4 years; Full Scale IQ=97.6±17.8; male/female ratio=4.5:1), their parents and siblings. Autistic traits were measured using the Developmental, Dimensional and Diagnostic Interview (3Di) and the Autism Diagnostic Observation Schedule (ADOS). An age and sex-standardized score was obtained for all subjects (6-60 years of age) from the Warrington Face Recognition Memory Test. Saliva, buccal cell or blood samples were collected from the participants for DNA extraction. 59 SNPs from the OXTR gene were genotyped using a Sequenom platform. Genetic associations were analysed using QFAM-PLINK for quantitative familial traits, implemented in BC-Gene. p-ACT was used to correct for multiple comparisons.

Results: We found SNP rs237887 is significantly associated with the face recognition memory endophenotype ($p=0.0001522$; corrected, $p\text{-ACT}=0.023$). The ancestral A allele of this SNP is associated with relatively impaired recognition memory in all family members. No transmission distortion was found in inheritance of this allele by probands. rs237887 is an intronic SNP located in a region that is predicted to interact with several transcription factors, suggesting a possible functional effect on OXTR gene expression.

Conclusions: This study implies evolutionary conservation of the role played by OXTR in social recognition memory, between animals (such as mice and voles) and humans. Our methodology emphasises the value of using age and sex-standardized endophenotypes to study genetic influences on cognitive traits relevant to ASD.

140.041 41 Relevance of Common CNVs for Autism Etiology. I. C. Conceicao*¹, C. Correia², B. Oliveira¹, J. Coelho³, C. Café⁴, J. Almeida⁴, S. Mougá⁵, F. Duque⁵, G. Oliveira⁵ and A. M. Vicente³, (1)*Center for Biodiversity, Functional & Integrative Genomics*, (2)*Instituto Gulbenkian de Ciência*, (3)*Instituto Nacional de Saúde Doutor Ricardo Jorge*, (4)*Hospital Pediátrico Carmona da Mota (HP) – Centro Hospitalar e Universitário de Coimbra (CHUC)*, (5)*Faculdade de Medicina da Universidade de Coimbra*

Background: Recent reports by the Autism Genome Project (AGP) consortium and other groups show that Copy Number Variants (CNVs), while individually rare, collectively may explain a

large fraction of the etiology of Autism Spectrum Disorders (ASD).

Objectives: The goal of this study was to establish the relevance for ASD etiology of potentially pathogenic CNVs identified in a Portuguese population sample by the AGP whole genome CNV analysis.

Methods: A total of 14218 CNVs were identified in 342 Portuguese probands (35 females, 307 males), genotyped by the AGP using the Illumina Infinium1M SNP microarray. We selected 1062 CNVs (present in 300 individuals) not overlapping by more than 50% with CNVs in 8000 controls from available databases and explored recurrence rates, genic content, regulatory elements, inheritance patterns and clinical correlations.

Results: The identified CNVs ranged from about 5 Kb to 3.7 Mb, with 54% being deletions. Larger CNVs (>500 Kb) were more frequently duplications than deletions. There were 65% genic CNVs, ranging from one gene (67% of all genic CNVs) to 22 genes in a single CNV. CNVs were inspected for recurrence rates and inclusion of ASD-implicated or candidate genes. Interesting CNVs were validated by qPCR, including *SHANK3* and *NRG1*. Although a large percentage of CNVs were present in only one individual (~94%), 13 or ~1.4% were common CNVs, defined as CNVs with a frequency of 1% or greater in the sample population. These CNVs were present in between 3 and 19 individuals, summing a total of 115 individuals (~38%) with common CNVs. Four CNVs not spanning any gene were identified in 3, 4, 5 and 17 individuals. The other nine CNVs include one gene or parts of it, namely *ATRX* (N=30 individuals), *DPYD* (N=22), *NRP1* (N=13), and *VAULTRC2* (N=5), with the exception of one CNV which affects four genes (*ATP7A*, *PGAM4*, *COX7B*, *MAGT1* - N=4) that are in tandem with *ATRX*. We further compared data for autistic traits in the parents (using the BAPQ and SRS questionnaires) with the type of inheritance (inherited vs de novo). We observed a significant excess of autistic traits in the fathers that transmitted a CNV, mainly in the "rigid" personality, which is defined as little interest in change or difficulty adjusting to change.

Conclusions: Here we highlight the importance of studying common CNVs for understanding the

etiology of autism. Also, we re-affirm the previously suggested presence of subthreshold autistic traits in the parents of children with ASD, in particular in patients with inherited CNVs. This exhaustive analysis of CNVs for clinical interpretation is necessary for the efficient translation of this knowledge into clinical practice, aiming at the development of molecular tools that may assist behavioral screening procedures for early diagnosis in ASD as well as genetic counseling.

Cognition and Behavior Program

141 Social Cognition - Theory of Mind

141.042 42 An Ethogram of Behaviors Guiding Dynamic Visual Scanning in 12-24 Month-Olds with Autism Spectrum Disorder. G. A. Marrinan*, A. Klin and W. Jones, *Marcus Autism Center, Children's Healthcare of Atlanta & Emory University School of Medicine*

Background: Previous research has demonstrated that two-year-olds with autism spectrum disorder (ASD) look more to mouths, bodies and objects when viewing video scenes of caregivers, while typically-developing (TD) toddlers look more to their eyes. Related research has shown that two-year-olds with ASD preferentially attend to physical contingencies, regardless of their social context. These analyses of visual fixation to discrete regions of interest suggest that toddlers with ASD attend more to physically salient aspects of a scene while TD toddlers preferentially attend to elements that have social adaptive value. These differential patterns of visual fixation align with findings within a separate but similarly motivated body of research investigating reward processing among individuals with ASD. Investigation of neural processing of reward among individuals with ASD suggests that individuals with ASD may process reward—particularly social reward—differently than typically-developing individuals, and may learn less than typically-developing individuals from socially mediated rewards. While summary analyses of fixation provide useful indices of differences between individuals with and without ASD, natural social interactions incorporate many dynamic and complex cues that are not limited to discrete regions of interest. The current study, rather than summarizing fixations in relation to regions of interest, aims to characterize functionally meaningful social actions that drive the attention of TD children but fail to capture the attention of children with ASD.

Objectives: This study aims to characterize functionally distinct elements within naturalistic stimuli that contribute to differences in dynamic visual scanning of children with and without ASD.

Methods: Eye-tracking data were collected as 12-24 month-old TD children (N = 28) and children with ASD (N = 48) viewed naturalistic videos of peer interactions. Children were matched on chronological age and non-verbal function. We quantified dynamic visual scanning using kernel density analysis, and the resulting measures of fixation density, at each moment in time, allowed us to model the allocation of visual resources for both groups throughout all video scenes. Using these measures, we tested for between-group differences in dynamic visual scanning. In parallel, we categorized functionally distinct categories of social behavior occurring in the videos by means of an ethnographic analysis. We then analyzed the catalog of behaviors during frames of the videos when the visual scanning of children with ASD and TD children differed significantly.

Results: Preliminary analyses suggest that socially functional elements of naturalistic video scenes, including gaze cues and intense facial expressions, serve as salient social signals to TD 12-24 month-olds, and drive their visual scanning more strongly than that of 12-24 month-olds with ASD. In contrast, preliminary results suggest that physical motions and vocalizations drive the scanning behavior of both children with ASD and TD children in a more similar fashion.

Conclusions: Socially relevant functional behaviors appear to drive attention more strongly among TD children than among children with ASD. The social and communicative outcomes of children with ASD may thus result from a divergent foundation of knowledge gained from atypical allocation of attention from an early age.

141.043 43 Arousal and Emotion Recognition in Music Among Youth with Autism Spectrum Disorders. K. Stephenson^{*1}, P. D. Chamberlain², D. N. Top¹, C. Nielson¹, E. M. Quintin³ and M. South¹, (1)*Brigham Young University*, (2)*Mikle South Research Lab*, (3)*Stanford University*

Background: Many studies have investigated the so-called amygdala theory of autism (Baron-Cohen et al., 2000) with evidence signifying that atypical amygdala function likely underlies high levels of anxiety in autism spectrum disorders

(ASD) (Amaral, Bauman, & Schumann, 2003).

The amygdala has been shown to be involved in the processing of emotions in music, specifically in fearful and sad emotions (Gosselin, Peretz, Johnsen, & Adolphs, 2007). However, Quintin, Bhatara, Poissant, Fombonne, & Levitin (2011) found that high-functioning autism spectrum disorder (ASD) adolescents did not differ from typical (TYP) adolescents in the accuracy of their behavioral ratings related to recognizing emotions in music.

Objectives: We extended the Quintin et al. study in two important ways: we measured physiological response during stimulus presentation, and we included an additional, younger participant group. We hypothesized that individuals with ASD (the ASD group) would show more arousal during scary music, relative to age- and IQ-matched typical controls (the TYP group).

Methods: There was a bimodal age distribution among participants. The younger group consisted of 50 participants ages 8-11 (M=9.92, 25 ASD).

The older group consisted of 50 participants ages 15-18 (M=16.8, 25 ASD). The task consisted of participants listening to 20 second musical clips in randomized order, including five of each emotion (sad, happy and scary). After each clip participants assessed the emotion and intensity.

Skin conductance response (SCR) was collected during the task with amplitude being analyzed according to the area under the curve following each stimulus.

Results: Behavioral measures of accuracy showed few reliable between-group differences. However, repeated measures ANOVA of the SCR showed that for the younger child group, there was a significant main effect for Emotion Condition, with the Scared condition showing higher arousal than the other conditions in both groups. There was no main effect for diagnostic group, but there was a significant Group x Condition interaction, indicating a substantially greater response to the scared condition in the ASD group. For the older teen group, there was a significant main effect for diagnostic group, as the mean SCR response for the ASD group (3.02 μ S) was significantly less compared to that of the TYP group (5.99 μ S) despite similar baseline arousal values. There was no main effect for condition and no significant Group x Condition interaction in the older sample.

The ASD group but not the TYP group showed a main effect for age with younger ASD children more responsive overall than the older cohort.

Conclusions: Schumann et al. (2004) suggested that in ASD the amygdala is larger and perhaps overactive in younger children, with growth slower compared to controls in adolescence. These data may reflect a functional consequence of this atypical growth pattern. Future research regarding emotion recognition in ASD should attend to probable developmental changes. Different psychophysiological responsiveness in the face of similar behavioral reports suggests atypical integration of cognitive and affective cues in ASD; the study of mechanisms underlying observable behavior may be useful for understanding known strengths and weaknesses in behavioral performance.

141.044 44 Atypical Interference Effect of Action Observation in Autism Spectrum Conditions. J. L. Cook^{*1}, D. Swapp², X. Pan², N. Bianchi-Berthouze² and S. J. Blakemore¹,
(1)University College London, (2)UCL

Background: Observing incongruent actions interferes with ongoing action execution. This "Interference Effect" is larger if the observed actor has human rather than robotic form (Kilner et al., 2003) and if the movement proceeds with biological motion rather than constant velocity motion (Kilner et al., 2007). The Mirror Neuron System (MNS) is a possible neural substrate for the Interference Effect (Blakemore & Frith, 2005). Little is known of the biological specificity of Interference Effects in Autism Spectrum Conditions (ASC).

Objectives: The current study used virtual reality to manipulate both actor form and motion and thus enable an investigation of the biological specificity of Interference Effects in ASC.

Methods: High-functioning adults with ASC and age-, gender- and IQ-matched typical controls performed horizontal sinusoidal arm movements whilst observing arm movements conducted by a virtual reality agent with either human or robot form, which moved with either biological motion or at a constant velocity. In another condition, participants made the same arm movements while observing a human. Observed arm movements were either congruent or incongruent with executed arm movements. An Interference Effect

was calculated as the average variance in the incongruent action dimension during observation of incongruent compared to congruent movements.

Results: Control participants exhibited an Interference Effect when observing real human and virtual human agent incongruent movements but not when observing virtual robot agent movements. Individuals with ASC differed from controls in that they showed no Interference Effect for real human, virtual human or virtual robot movements. Interference Effects did not significantly vary according to the type of motion (biological or constant velocity) observed.

Conclusions: The current study demonstrates atypical Interference Effects in ASC. Given that the MNS is a plausible neural correlate of the Interference Effect the current results can be considered consistent with the broken MNS hypothesis of ASC (Ramachandran & Oberman, 2006). However, more recent theories suggest that rather than the MNS per se being 'broken' in ASC it may be that *modulation* of the MNS is atypical (Cook, Barbalat, Blakemore, 2012; Hamilton, 2008; Spengler et al., 2010; Kana et al., 2011). For instance, social priming has been demonstrated to elevate imitation in typical adults but not in adults with ASC (Cook & Bird, 2011). It may be that, in the current experiment, the human form present in the human agent acts as a 'pro-social prime' for typical individuals but not for individuals with ASC. Atypical social modulation of this sort may result in an elevated Interference Effect for the control group but not for the ASC group. Thus the current results are consistent with both broken MNS and atypical modulation accounts of ASC.

141.045 45 Atypical Visual Processing in ASD As A Global Deficit or Local Bias: A Meta-Analysis. R. Van der Hallen*, K. Brewaeys, W. Van den Noortgate and J. Wagemans, University of Leuven (KU Leuven)

Background: 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. In spite of influential theories like the Weak Central Coherence (WCC) and the Enhanced Perceptual Functioning (EPF) account and a great deal of

research inspired by them, the atypical visual processing profile of individuals with ASD remains only partly understood. The debate focuses in particular on whether differences in autistic visual perception should be conceptualized as either a local bias or a global deficit. Proper quantitative reviews of the available data, in which the overall effect size of each study is assessed and the influence of potential moderators is investigated, are lacking.

Objectives: We combined all available experimental data on local and global visual processing in ASD from 1983 till 2011 through meta-analytic techniques, and (a) assessed whether the available data are in favor of the hypothesis of superior local processing or the hypothesis of inferior global processing, in individuals with ASD compared to typically developing (TD) controls, (b) evaluated the conceptualization of local and global visual processing in different paradigms and measures, and (c) evaluated which moderator variables rule the diversity within the literature.

Methods: A systematic literature search was performed. All data of the 44 selected articles were coded and transformed to the standardized mean difference metric d and used in a linear three-level random effects model, accounting for random sampling fluctuation, between-outcome variance and between-study variance. Further analyses carefully extended the model by including one or more of nine moderator variables, comprising ASD subtype, type of control group, sample size, gender, age, IQ, experimental paradigm or task, dependent variable, and assumed direction of group difference (e.g. enhanced local versus reduced global).

Results: Overall, we found no significant performance difference in visual processing between individuals with ASD and controls. Yet, analyses investigating the individual or combined influence of moderator variables showed significantly reduced performance of the ASD group for tasks inducing a global processing advantage (especially as measured by reaction times), but no effect for task elements inducing a local processing advantage (nor when accuracy measures were used). The moderator variables age, gender and IQ yielded mixed results,

whereas the specific subtype of ASD did not have any effect.

Conclusions: The results of this meta-analysis favor the evidence for a deficit in global visual processing in ASD rather than an advantage in local processing in ASD. Though several important moderator variables have been included in the study, further research is necessary to identify more clearly which (other) moderator variables are at play and how they influence visual processing abilities in individuals with ASD versus controls.

141.046 46 Behavioral Study On Perception of Emotional Speech in Individuals with Autism Spectrum Disorders. K. Matsumoto^{*1}, T. Sugiyama¹, C. Saito², S. Kato¹, K. Kuriyama¹, K. Kanemoto³ and A. Nakamura⁴, (1)*Aichi Children's Health and Medical Center*, (2)*Obu Dementia Care Research and Training Center*, (3)*Aichi Medical University*, (4)*National Center for Geriatrics and Gerontology*

Background: Smooth communication requires not only understanding of linguistic meaning, but also interpretation of emotions based on nonverbal information such as facial expressions and prosody. Individuals with autism spectrum disorders (ASD) have difficulty holding smooth conversations due to their inability to perceive others' emotions during communication. Previous studies on emotion perception in ASD have primarily been conducted from a visual perspective such as perception of expressions, and few studies have been conducted from an auditory perspective with a focus on the ability to perceive emotions conveyed in speech.

Objectives: To elucidate the characteristics of speech perception in ASD from a behavioral perspective.

Methods: Subjects were 12 individuals with ASD not receiving drug therapy and 12 typical development aged between 10 and 15 years. Diagnosis was made in person using the DSM-IV. The sex ratio, age, and IQ did not significantly differ between the two groups. The experiment was conducted using Presentation (Neurobehavioral Systems, Inc., USA). Speech stimuli consisting of words and SVO (Subject + Verb + Object) sentences conveying three types of emotions (happy, anger, normal voice) were provided to subjects, who were given the tasks of semantic perception, which involved identifying

the semantic content of the speech stimulus, and emotion perception, which involved identifying the emotion associated with the speech. On each task, subjects were asked to respond by pressing one of three buttons, and the correct response rate and response time were compared between the groups.

Results: On the emotion perception task, no intergroup differences were seen in the correct response rates for both the word and SVO sentence stimuli, but the response time was significantly longer in the ASD group (mean, approximately 200 ms; $P < 0.05$). On the semantic perception task, the ASD group had a significantly lower correct response rate (0.95 ± 0.04 vs. 0.99 ± 0.02 ; $P < 0.005$) as well as a longer response time when an SVO sentence stimulus for anger was presented.

Conclusions: I-M Eigsti (2011) suggested that sites for perception of emotional speech may differ between ASD and TD. In the present study, individuals with ASD took longer than TD to process—in other words, to perceive and output—the emotions expressed by the speaker. This finding suggests that individuals with ASD and TD have different perception processes. The results also indicate that individuals with ASD may have difficulty correctly perceiving the speaker's intentions when they are expressed with an unpleasant emotion. In order to enable individuals with ASD to improve their perception ability, it may be important for those providing support to individuals with ASD to pay careful attention to the emotions conveyed in verbal speech during conversations.

141.047 47 Children with Autism Following Teacch Like School: Evolution of Their Social Cognition Through One Year and a Half. E. Thommen*, S. Wiesendanger, B. Carier-Nelles and A. Guidoux, *University of Applied Sciences Western Switzerland*

Background:

Social cognition in autism has been extensively investigated during the last thirty years. Children with autism are generally less good than control groups in theory of mind's tasks (Yirmiya et al. 1998; Peterson, et al. 2005). Also, emotional understanding is also regularly presented as deficient (Baron-Cohen, 1993; Celani et al., 1999; Thommen et al., 2004).

Objectives:

Longitudinal data and evaluation of these these abilities are yet in elaboratio. The aim of our presentation is to follow the development of social cognition through time.

Methods:

We evaluated twenty eight children with autism (5- to 15-years old, $M = 10;6$) with the French version of the Tom Storybooks (Blijd-Hoogewys at al. 2003) and French version of the TEC (Test of Emotion Comprehension, Pons & Harris, 2005). All are evaluated with the Wechsler Nonverbal Scale, the E.CO.S.SE (French equivalent of TROG) and diagnosed with the DSMIV. This evaluation is repeated three times during one year and a half. A comparison group of 64 children aged from 5- to 9-years old spent the same test battery in order to compare the results to typical development.

Results:

Results reveal that children with autism are able to attribute simple mental state to story characters. They generally understand what a belief is as well as belief changing, but they are specially impaired in false belief tasks. Longitudinal data shows improvement in their abilities, but they do not reach the level of children of their age

Conclusions:

Implications from this research are multiple. First, the sensibility of the Tom Storybooks and the TEC to evaluate the evolution in children's theory of mind will be important for testing progress. Second, the evaluation of the developmental course of theory of mind understanding in children with autism is useful for those who try to understand this process and teach children on these abilities. Third, the comparison with control groups will confirm the specific difficulties of theory of mind comprehension in person with autism spectrum disorder.

141.048 48 Components of Perspective Taking in Autism. A. B. de Marchena*¹, R. García-Pérez² and I. M. Eigsti¹, (1)*University*

Background: Children with autism have well-known limitations in their ability to imitate and to adopt others' perspectives (Garcia-Perez, Hobson & Lee, 2008, Hobson & Hobson, 2008; Meyer & Hobson, 2004). However, they do show areas of strength within this complex domain (Hobson & Lee, 1999). Specifically, children with autism are less likely to adopt others' *attitudes* than to imitate specific *actions*. This discrepancy may suggest that children with autism have limitations in their propensity to identify with the attitudes and feelings of others, resulting in a tendency to adopt some aspects of others' perspectives (e.g., explicit actions) but not all (e.g., implicit attitudes).

Objectives: The goal of this pilot study was to determine what features of others' perspectives are spontaneously adopted by children with autism. We specifically compared adoption of the *actions* enacted by others with their *attitudes* (i.e., emotional valence). Further, we divide actions into *motor* behaviors (i.e., pantomime) and *verbal* behaviors (i.e., non-speech vocalizations). We expect that this analysis will shed light on relative strengths and weaknesses within the domain of perspective taking and imitation in autism.

Methods: Participants were 9 children with autism and non-autism developmental delays living in Madrid, Spain. All measures were conducted in Spanish. Participants acted out six different scenarios featuring transitive actions (e.g., "act like a monkey eating food"). On each trial, following the child's spontaneous enacting of the scenario, the experimenter modeled the scenario herself, including a specific *action*, *sound*, and *attitude*, then asked the child to enact the event again. The action was the same for all six trials across participants. The attitude and sound, which reflected that attitude, were counterbalanced, such that half of the participants saw the experimenter enact one attitude and sound for a given trial (e.g., monkey is disgusted by what he is eating) and the other half saw a contrasting attitude (e.g., monkey loves what he is eating). We are interested in comparing participants' enacting of the action, which requires imitation but minimal role taking, with their

enacting of the sound and attitude, which require progressively higher degrees of role taking.

Results: 4 children with autism were able to complete all study procedures (Mean chronological age = 10.0 years, Mean verbal mental age = 6.3 years). On average, action, sound, and attitude appeared to be comparably challenging, with successful performance at 2.25, 2.25, and 2.5 trials (respectively, out of 6). Participants varied in terms of their individual abilities; while some participants were most skilled at adopting the experimenters' actions, others adopted her attitude most effectively. The range of performance observed in this small sample suggests that our task is appropriate for studying multiple components of perspective taking in this population.

Conclusions: Imitation and perspective taking are critical targets autism interventions. The current pilot study is in its early stages, but our results suggest that breaking perspective taking into action, sound, and attitude in this way may help shed light on the different aspects of perspectiv

141.049 49 Cross-Situational Word-Face Learning in Children with ASD. H. Akechi^{*1}, Y. Kikuchi², Y. Tojo², H. Osanai³ and T. Hasegawa⁴, (1)Tokyo Denki University, (2)Ibaraki University, (3)Musashino Higashi Gakuen, (4)The University of Tokyo

Background: It was reported that children with autism spectrum disorder (ASD) have difficulty in learning words via social cues (e.g., speaker's eye gaze; Baron-Cohen et al., 1997). However, some children with ASD acquire vocabularies as rich as typically developing (TD) children. One of potential efficient strategies is a cross-situational learning, which is a mechanism for learning the words across multiple trials even when there is no definite cue for the word-object correspondence in one trial. We previously demonstrated that the cross-situational learning is an efficient strategy for children with ASD (Akechi et al., 2012, IMFAR). Children with ASD also reportedly have difficulty in face memory (Weigelt et al., 2011). However, whether cross-situational learning is also efficient to learn associations between words and faces in ASD was not investigated yet.

Objectives: To investigate whether children with ASD learn words-faces association effectively using cross-situational learning.

Methods: Participants consisted of 20 children with ASD (mean age 9.1; range 6-12) and 20 TD children (mean age 9.1; range 7-12), who were matched on verbal mental age (VMA). There were 6 novel words and 6 novel faces. In the training phase, two novel faces were presented on the monitor and two corresponding novel words were presented via the loudspeaker in each trial. There is no definite cue for the word-face correspondence in one trial. Each word-face pairs was presented 10 times. In the test trials, two faces and one word were presented and the participant was asked which face is the referent. Each face was presented twice as a target and twice as a non-target. Thus, there were 12 test trials in total. The procedure was same as the previous study (Akechi et al., 2012), except that the objects were replaced with faces.

Results: The performance in the test trials in both the ASD ($p < .005$) and the TD group ($p < .001$) were above chance level (6/12 = 50%). However, there was a significant difference between groups in the performance ($p < .05$). Additionally, the analysis across experiment showed that the performance of children with ASD in the present study was lower than that of those in the previous study ($p < .005$) but there was no significant difference in the TD children ($p > .05$).

Conclusions: Results suggest that children with ASD can learn novel face-word associations using cross-situational learning, but compared to TD children, they have difficulty learning the name of human face cross-situationally.

141.050 50 Demands in Reflecting about Another's Intentions
Modulate Vicarious Embarrassment in Autism Spectrum Disorders. F. M. Paulus*¹, I. Kamp-Becker² and S. Krach²,
(1)Philipps-University Marburg, (2)Philipps-University Marburg

Background: The affective responses to another person's condition are not fully independent of the abilities to reflect about another's thoughts and intentions. This is highly relevant also for high-functioning individuals with ASD who have considerable difficulties in reading the intentions of others.

Objectives: Using a novel paradigm to induce vicarious embarrassment as a form of social pain, we aimed to demonstrate that ASD may indeed modulate the affective response to another

person's state. We predicted that the vicarious embarrassment of high-functioning individuals with ASD should specifically decline in context of situations that require understanding others' intentions and reflecting on the motives that cause another's actions.

Methods: The ASD group consisted of 32 young male adults who had a confirmed ICD-10 diagnosis of high-functioning Autism, Asperger Syndrome, or Atypical Autism. The control group was group-matched for age (ASD: M = 20.19, SD = 2.82, CG: M = 21.44, SD = 2.31), gender, and verbal IQ (ASD: M = 114.47, SD = 15.47, CG: M = 114.33, SD = 12.38). Vicarious embarrassment was examined with a selected set of previously validated stimuli. Stimuli consisted of 30 German sentences that described vicarious embarrassing situations and 10 neutral scenarios. All vicarious embarrassment situations showed a protagonist who either *accidentally* or *intentionally* transgressed a social norm in public and participants rated their own vicarious embarrassment in response to the situation on a scale from 1 ("not at all") to 7 ("very strong").

Results: Results indicated statistically significant main effects for Group $F(1,62) = 5.27, p = .03$ and Situation $F(2.53, 156.59) = 14.33, p < .001$. Importantly, the two-way interaction between Group and Situation was statistically significant with $F(2.53, 156.59) = 4.34, p < .01$. Post-hoc comparisons indicated that the effects were driven by the ASD group who showed similar vicarious embarrassment in response to observing another's *accidental* norm transgressions but significantly reduced vicarious embarrassment when observing another who *intentionally* violated social norms. Further, vicarious embarrassment was significantly correlated with self-reported empathy in the ASD group ($41 < r < .46, ps < .05$).

Conclusions: The results provide first evidence for vicarious social pain experiences in high-functioning individuals with ASD. High-functioning individuals with ASD indeed reported vicarious embarrassment as do non-autistic controls, however, their vicarious embarrassment significantly declined when it was necessary to understand others' intentions and reflecting on the motives that cause another's actions. These results demonstrate that the ASD associated impairments have considerable impact on the

affective responses towards another person's state in the context of complex social scenarios. This is also in line with earlier reports of children with ASD to have difficulties to understand the concept of deception and a very recent study that showed individuals with ASD to have difficulties to integrate the intention of another's actions when judging the morality of another's behavior. The present study thus contributes to a more comprehensive understanding of how ASD influences the diversity of empathic processes in the social, everyday life environment they are embedded in.

141.051 51 Developmental Trend in Theory of Mind in School-Aged Japanese Children of Typical Development and with High-Functioning Autism Spectrum Disorder: Application of the Animated Version of the Theory of Mind Test. H. Fujino*, *Tokyo Gakugei University*

Background: We developed an animated version of the theory of mind (ToM) test, and applied it to Japanese children. This assessment tool includes five ToM tasks based on 'Sally-Anne', 'Smarties', 'Strange Stories: White Lie', 'Sabotage/Deception' and the second-order false belief 'John and Mary'.

Objectives: This study investigated the development of ToM in Japanese students with typical development (TD) and in those with high-functioning autism spectrum disorder (ASD) applying this ToM test.

Methods: Elementary school children from the second to fourth grades (age 8–10), including 70 TD children and 63 ASD children with normal intelligence, participated in the study. Among the ASD children, the average verbal IQ was 106.5 (range 85–138) and the average performance IQ was 102.8 (range 85–122) on the WISC-III. The ToM tasks were presented to the participants via audio, letters and animations using a PC display and speaker. The passing number of the tasks were scored (0–5). To pass each task, all sub-questions including control questions had to be correctly answered.

Results: The average scores (standard deviation) of the ToM tasks were 4.32 (0.85), 4.54 (0.66) and 4.71 (0.46) for TD children, and 2.32 (1.46), 3.29 (1.37) and 4.21 (1.12) for ASD children of the second, third and fourth grades, respectively. A two-way analysis of variance (ANOVA) (3 (Grade: second versus third versus fourth) × 2

(Group: ASD versus TD)) was conducted. The interaction between age and presence of ASD was significant ($F(2,127) = 5.11, p < .01$). The simple main effect of grade was significant only in ASD children ($F(2,127) = 14.92, p < .001$). The ToM performance in the second grade was significantly lower than that in the third grade, and was significantly lower in the third grade than that in the fourth grade. The simple main effect of the presence of ASD was significant in the second ($F(1,127) = 44.58, p < .001$) and third grades ($F(1,127) = 44.58, p < .001$). The ToM performance in ASD children was significantly lower than that in TD children in the second and third grades. The logistic regression analysis indicated that the ToM score was a significant predictor of ASD in the second ($B = -1.38, Wald = 12.97, p < .001, odds ratio = 0.25$) and third grades ($B = -1.55, Wald = 9.67, p < .01, odds ratio = 0.21$), but was not significant in the fourth grade. The predictive values of ASD were 78% and 73% in the second and third grades, respectively.

Conclusions: These results suggest that the animated version of the ToM test can detect ToM problems in ASD children until the third grade. However, it cannot accurately detect these problems in the fourth grade. Therefore, the results on this ToM test should be evaluated carefully, particularly when applied as an assessment tool among children in the fourth grade or higher. Happé (1995) suggested that the verbal mental age of nine is critical for passing ToM tasks. Our results also support this finding.

141.052 52 Does Eye Contact Enhance the Accuracy of Hand Imitation in Children with ASD?: An Eye-Tracking Study. Y. Kikuchi*¹, Y. Tojo², H. Osanai³ and T. Hasegawa⁴, (1)*Japan Society for the Promotion of Science*, (2)*Ibaraki University*, (3)*Musashino Higashi Gakuen*, (4)*The University of Tokyo*

Background: Children with autism spectrum disorder (ASD) had difficulty in imitation and they showed reduced attention to a model's face when observing hand actions (Vivanti et al., 2008). We previously demonstrated that children with ASD imitated hand postures more accurately when eye contact was established in a live task (Kikuchi et al., IMFAR 2012). However, their fixation pattern still remains unknown. Also, it is important to investigate whether this better performance by eye contact is due to live presentation or not.

Objectives: By using an eye-tracker, we investigated whether children with ASD performed more accurately in imitation of video model's hand postures when eye contact was established.

Methods: Participants consisted of 21 children with ASD (mean age 9.3 years; range 6-12 years) and 24 TD children (mean age 8.3 years; range 6-12 years) matched on the verbal mental age. Eight unimanual postures and those 180° rotated postures were presented. In Face block, participants were asked to look at the model's face and to imitate the hand postures. In Object block, the model wore a colorful flower on the top of her head and bowed to hide her face. Participants were asked to look at the flower and to imitate the hand postures. Form (e.g. number of fingers, correct position of fingers) and Orientation (a child's palm was to the model when the model's palm to the child, and vice versa) were analyzed.

Results: Although the performance in the display presentation was less accurate than that in the live presentation, we replicated our previous results. On both Form and Orientation, children with ASD performed less accurately than TD children ($p < .05$), but the performance was better in Face condition than Object condition across the group ($p < .05$). In Orientation, the interaction between group and condition was significant ($p < .05$); the performance of Orientation was better in Face condition than Object condition in children with ASD ($p < .01$) but not in TD children ($p > .7$). In children with ASD, the ratio of the Face/Hand fixation time was larger than that of the Object/Hand fixation time ($p < .05$).

Conclusions: In the display presentation, children with ASD also imitated the hand postures more accurately when the eye contact was established.

141.053 53 Effects of Theory of Mind Impairment On Intelligence Testing in Low Functioning Individuals with ASD. A. San José*¹, F. Happé² and R. D. Booth¹, (1)King's College London, (2)Institute of Psychiatry, King's College London

Background:

The Theory of Mind (ToM) impairment is one of the best-studied theories explaining ASD. However, the severity in which such deficit may

impact in other cognitive abilities remains largely unexplored. Scheuffgen et al. (2000) found that low-functioning individuals with ASD (as measured by the Wechsler scales of intelligence) performed as well as TD controls in a simple Inspection Time (IT) task, known to correlate around -.50 with intelligence in TD individuals (Grudnik & Kranzler, 2001). Following the Minimal Cognitive Architecture model of intelligence (Anderson, 1992), the authors proposed that g (as measured with an IT task) remains intact in individuals with ASD, alongside a damaged ToM external module necessary to perform typically. A replication by Wallace et al. (2009) found this to be the case in low-, but not high-, functioning individuals with ASD, suggesting an increasing disparity between IT and intelligence with decreasing IQ.

Objectives:

In order to provide the appropriate level of education and support, it is paramount to know whether psychometric or cognitive tools accurately reveal the intellectual potential of low-functioning individuals with ASD and what variables may mediate any discrepancies. This study set out to explore the impact of ToM deficits on the discrepancy between cognitive and social psychometric intelligence measures in ASD. Furthermore, it was examined whether this discrepancy is specific to ASD or an expression of their global Intellectual Disability (ID).

Methods:

25 individuals with ASD+ID and 35 with ID alone (CA 8 to 19 years) completed the Coloured Progressive Matrices (CPM) and a visual IT task. Due to the severity of their intellectual impairment, materials for both tasks were adapted to match their ability levels. ToM measures consisted of the Penny Hiding Game, the updated Interactive and Active Sociability scales and the Vineland scales of adaptive behaviour. Lastly, they were assessed on the British Picture Vocabulary Scales (BPVS).

Results:

Overall, the ASD group performed faster on the IT task than the ID group even when IQ-matched

(14 ASD and 14 ID; $z = 2.09, p = .04$). CA was highly correlated with VIQ (from BPVS; $r = -.72; p < .001$) and PIQ (from CPM; $r = -.81; p < .001$) in the ID group but not in the ASD group. Supporting predictions, a discrepancy between crystallized (VIQ) and fluid measures of intelligence (IT) correlated moderate to highly with all social measures (including those measuring ToM; all $p < .001$) in the ASD group, but not in the ID group. Also, a strong directionality effect (higher PIQ than VIQ) was found in the ASD group.

Conclusions:

The findings suggest intact processing speed and potential intelligence in ASD, which is not tapped by socially mediated tools, or measures of crystallized intelligence, and supports previous studies where ASD individuals outperformed IQ-matched ID individuals in the IT task. Furthermore, the strong directionality of the ASD group towards the PIQ in contrast to the ID group supports the strong differences between groups in terms of IQ profiles. This could have future implications in which ASD is assessed and conceptualized.

141.054 54 Emotion in the Voice, Emotion in the Eyes, and Emotional Intelligence and Their Relationship with Autistic Traits. M. E. Stewart^{*1}, M. Ota², C. McAdam¹, K. De Busk², S. Peppe³ and J. Cleland³, (1)*Heriot-Watt University*, (2)*University of Edinburgh*, (3)*Queen Margaret University*

Background:

People with Autism Spectrum Condition (ASC) are known to exhibit emotional processing patterns that are different from typically developing individuals. Such differences have been observed primarily in two areas: speech prosody and facial expressions. A central question for these differences in performance is whether they reflect problems in modality-specific processing (e.g., speech or face) or a common underlying cognitive difference. We test this in a relatively homogeneous group in which linguistic skills and IQ can be assumed to be less variable than that of the ASC population, a group of students who vary on autistic trait scores.

Objectives:

To examine 1) whether autistic traits have independent effects on emotional processing in speech prosody and facial expression, and 2) whether both of these domains can be related to models of general emotional understanding, in particular, Theory of Mind and Emotional Intelligence.

Methods:

116 students were recruited, consisting of 80 females and 36 males, with a mean age of 21.1 years, (s.d.= 3.4, range 17-37). Participants completed the Autism-Spectrum Quotient (AQ; Baron-Cohen, Wheelwright, Skinner, et al., 2001); Swinburne University Emotional Intelligence Test (SUEIT; Palmer & Stough, 2001); Reading the Mind in the Eyes (RMET; Baron-Cohen et al., 2001); and tests of emotional prosody (Stewart et al., 2013). The emotional prosody test consisted of two parts. In one, the prosodic information was part of sentences which sometimes signalled emotional states through their semantic/lexical content (congruent with the meaning of the sentence; incongruent; or neutral). In another, the same sentences were vocalisations ('mmm') so that only the prosodic cues were available to the listener.

Results:

The AQ correlates highly with emotional intelligence ($r=-0.57, p<0.01$) and with the performance in three of the conditions in the test of emotional prosody (incongruent, $r=-0.43, p<0.01$; neutral $r=-0.26, p<0.05$; and "mmms", $r=-0.57, p<0.05$), but not in the congruent condition. There is no correlation between AQ and the Reading the Mind in the Eyes task (RMET). There is also no relationship between emotional intelligence and the other emotional measures, nor is there any relationship between the RMET and the other emotional measures. However, verbal IQ correlates with the RMET ($r=-0.29, p<0.05$).

Conclusions:

First, the Autism-Spectrum Quotient in neurotypicals was related to identification of emotions based on speech, but this effect was not related to their ability to interpret emotional

values in the semantic content of the linguistic stimuli. Second, a measure of general emotion processing capacity (EI) showed no connection with identification of emotion in speech even though it was correlated with AQ. Third, in contrast to the performance in the speech task, which correlated with AQ, no connection was revealed between AQ and the performance in the emotion recognition from the eyes. The results are suggestive of a modality-specific explanation of the emotional processing difficulties in found in ASC. However, our study did not yield conclusive evidence against the view that a more general deficit in understanding emotional states underlies the processing of speech and faces in ASC.

141.055 55 Emotion, but Not Identity Matching, Is Affected by IQ in Autism. N. Mahalalel*¹ and Y. Levy², (1)*The Hebrew university of Jerusalem*, (2)*The Hebrew University of Jerusalem*

Background: Contrasting results are reported with respect to performance on tasks of face and emotion recognition in ASD (e.g. Harms, et.al. 2010; Weigelt, et.al 2012). Jointly with the lack of focus on faces, in particular on the eye region, during interpersonal interactions, deficient face and emotion recognition are thought to affect the social competences of individuals with autism. Recent research points to interactions between processes of face and emotion recognition in healthy individuals. A study of populations with cognitive deficits showed facilitation of same-identities on emotion matching task, but lack of facilitation of same-emotions on identity matching (Levy, et.al 2011). This result confirms earlier reports of difficulties in emotion recognition encountered by populations with cognitive impairments (e.g. Williams, et.al 2005). Such difficulties are not surprising, given that recognition of expressions is a conceptual as well as a perceptual task, requiring categorization and social understanding and hence affected by cognitive impairment.

Objectives: Difficulties in social interactions characterize people with autism at all levels of cognitive functioning. Are these impairments reflected in the general pattern of performance of people with autism on face and emotion recognition tasks? Alternatively, will poor performance on expression tasks characterize low functioning people with autism, yet not people

with autism of normal IQ? Will a similar difference in performance characterize identity tasks?

Methods: Subjects in the HI group were 24 males with autism, IQ > 85. Subjects in the LI group were 24 males with autism, IQ < 70. Mean age of the participants was 24.4 years. The groups were matched for vocabulary on the PPVT-3. Participants were tested on a matching paradigm, in which identities and expressions were manipulated simultaneously as the relevant or irrelevant dimensions. In the Identity task subjects were required to match faces with same or different expressions. In the Expression task subjects had to match expressions of same or different faces. Verbal responses were not required.

Results: Group performance was analyzed using a mixed-model ANOVA with repeated measures. In the Identity matching task, GROUP was the between-subjects variable (HI, LI) and the within-subject factors were CONGRUENCE (congruent, incongruent) and EXPRESSION (happy, disgusted). GROUP X CONGRUENCE interaction was found, as only in the HI accuracy in the congruent condition was higher than in the incongruent condition; that is, emotion recognition facilitated identity matching solely in the HI. The Expression matching task had four expressions – happy, disgusted, sad and angry. Two main effects (GROUP, CONGRUENCE) were found, as the HI group and the congruent condition yielded better accuracy; that is, facilitation of emotion matching by same-identity was not affected by IQ differences.

Conclusions: Results point to the effects of cognitive impairment on expression matching in autism. IQ did not have a similar effect on identity matching. The LI group is thus similar to other populations with intellectual handicaps, in whom the social-conceptual nature of emotion matching is impaired. These results support the decision in the forthcoming DSM-V to consider intellectual level as external to the diagnosis of autism and points to directions in intervention.

141.056 56 Emotional Inferencing in the Reading Comprehension of Persons with Autism. M. J. Tirado Maraver* and D. Saldaña Sage, *Universidad de Sevilla*

Background: Persons with Autism Spectrum Disorders (ASD) often have problems in reading

comprehension associated with difficulties in inferencing. However, previously published studies provide conflicting data: studies using off-line tasks tend to find differences between the autism and control groups, whereas others using on-line measures do not. In addition, most tasks used in the literature assess local coherence more often than global text comprehension.

Objectives: With this series of experiments we aimed at exploring if reading difficulties persist when tasks require global coherence, specifically in the construction of a situation model based on the emotional status of the main character in a story. We also wanted to compare the performance of readers with autism on both types of measures (off- and online) to poor comprehenders (PC) and typically developing readers (TD).

Methods: Three equal sized groups of adolescents and young adults with ASD, PC, and TD ($N = 66$), were matched on chronological age, reading speed, working memory, and gender. They all had a normal nonverbal IQ. There were significant differences in reading comprehension between the control group and the two other groups.

Three experiments were carried out in which it was necessary to construct a situation model that included determining the emotional status of the protagonist. In Experiments 1 and 2 (on-line tasks), participants were presented with stories that included a target phrase that explicitly mentioned an emotion. This sentence could be consistent or inconsistent with the previous text. In Experiment 1, the target appeared immediately after the text necessary to infer the emotion, while in Experiment 2 we included filler sentences between the section of the text describing the implicit emotion and the target. In Experiment 3 (off-line), the emotion was not made explicit in any target sentence. Participants were asked to rate four emotions according to how well they described the feelings of the main character in the story.

Results: In Experiments 1 and 2, mean reading times (RT) for targets were significantly longer when the explicit emotion was inconsistent with the previous text. However, in the first experiment no interaction of consistency and group was found. In the second, there was an interaction

effect, resulting from no differences between consistent and inconsistent target RTs in the PC group. In Experiment 3, there was a significant main effect of group in accuracy scores. Participants with ASD had the lowest accuracy rate of all three groups.

Conclusions: Although poor comprehenders show difficulties in the production of automatic inferences when these involve increased working memory load, this is not the case for readers with autism. However, ASD readers do show impaired performance in tasks that require the use of information available in the text in order to respond to explicit questions. The results point to difficulties in the comprehension of ASD readers that could be specific and different from poor comprehenders.

141.057 57 Eye Movements in Scene Perception During Cognitive Perspective Taking. S. K. Au-Yeung^{*1}, J. K. Kaakinen² and V. Benson¹, (1)*University of Southampton*, (2)*University of Turku*

Background:

The theory of mind deficit hypothesis (Baron-Cohen, 2001) postulated that social communicative deficits in Autism Spectrum Disorder (ASD) are the result of the inability to infer the mental states of others. Although reduced performance in a range of theory of mind tasks has been shown empirically in the ASD population, there are processing differences in other cognitive domains that are not accounted for. Minshew and Goldstein (1998) proposed that ASD is the result of disordered complex information processing across cognitive domains.

Objectives:

The current study was set up to investigate: a) if individuals with ASD were able to take on the psychological perspective of others during scene viewing, and b) if there were any subtle processing differences between TD individuals and ASD individuals that could be inferred from a range of eye movement measures.

Methods:

We recorded the eye movements of typically developed adults (TD, $n = 15$) and adults with ASD

(ASD, $n = 15$) while they inspected household scenes with two simple non-perspective taking instructions (e.g., look for valuable objects/features of the house that need fixing) and two complex perspective-taking instructions (e.g., imagine that you are a burglar/repairman).

Results:

Like the TD group, the ASD group modulated what they looked at and for how long depending on the perspective that they had in mind whilst performing the task. There were no differences in almost all eye movement measures between the two groups for the simple non-perspective taking instructions, and also the complex burglar perspective. However, there was a reduced or absent perspective effect for the ASD group for the repairman perspective in several eye movements measures. Specifically, the eye movement measures for the repairman perspective-taking task revealed subtle processing differences between the groups that were related both to initial orienting, and to the overall processing of perspective relevant items. The data suggest that the ASD group found the task more ambiguous when trying to identify relevant targets from irrelevant targets for the repairman perspective.

Conclusions:

In contrast to the traditional theory of mind view of ASD (Baron-Cohen, 2001), participants with ASD in the current study were able to take on the perspective of others. However, the perspective effects for several eye movement measures were weaker in ASD compared to TD for the repairman, but not the burglar perspective. The present results together with our previous findings (Benson, Castelhana, Au-Yeung, & Rayner, 2012) suggest that resolving ambiguity is a defining feature of deficits in complex information processing in ASD (Minschew & Goldstein, 1998).

141.058 58 Eye-Tracking and Upright and Inverted Face Recognition Performance in Adults with an Autism Spectrum Disorder. D. Hedley*¹, R. L. Young² and N. Brewer², (1)*Nationwide Children's Hospital and The Ohio State University*, (2)*Flinders University of South Australia*

Background: This study examined the Face Inversion Effect (FIE) in individuals with an

Autism Spectrum Disorder (ASD), and whether difference in attention to the mouth and eyes affects overall face recognition performance. The term FIE describes the effect on performance of inverting stimuli during a face recognition task. Inversion is thought to disrupt holistic face processing and forces reliance on inner face features. There is some evidence that individuals with an ASD may not be affected by inversion to the same degree as persons without an ASD (Hobson et al., 1988; McPartland et al., 2004). Some studies, however, indicate that older or higher functioning individuals with ASD are affected by inversion (Lahaie et al., 2006; Scherf et al., 2008). Interestingly, eye-tracking studies have found that individuals with an ASD spend less time fixating on the eyes and show increased attention to the mouth region (Corden et al., 2008; Pelphrey et al., 2002; Spezio et al., 2007). It is not known how this might impact inverted face recognition.

Objectives: To examine the FIE in adults with an ASD. We predicted participants with an ASD would be less affected by face inversion than non-ASD participants. We used eye-tracking to examine between-group differences in attention to the eyes and mouth.

Methods: We compared upright and inverted face recognition performance for 26 participants with an ASD ($M_{\text{age}} = 28.91$, $SD = 9.49$ years) with that of 33 ($M_{\text{age}} = 24.99$, $SD = 9.98$ years) age and IQ matched non-ASD participants. Stimuli were 72 (36 targets) male faces cropped to reveal the inner face only. Upright and inverted images were presented on a Tobii eye-tracker which recorded eye-movements. A study phase was followed by a recognition test. Eye-movements, RT and recognition performance were examined.

Results: Face recognition was significantly better for upright compared to inverted faces, and non-ASD participants performed better than participants with an ASD. A non-significant interaction ($F < 1$) between diagnosis and inversion suggested that both groups were affected by inversion. Participants with an ASD did not, therefore, show an RT advantage for inverted faces compared to non-ASD participants. Effect size analysis of RT differences between inverted and upright faces did, however, hint at a larger advantage for upright compared to inverted faces

for non-ASD participants (77 ms, $d = .28$) compared to participants with an ASD (6 ms, $d = .01$). Both groups directed more fixations to the eyes than the mouth, irrespective of image orientation, and no between-group differences were identified for eye-movement measures. Increased attention to the eyes was not associated with better recognition performance.

Conclusions: Recognition and RT results provided evidence that adults with an ASD are affected by face inversion, although non-ASD participants showed a greater, albeit non-significant, RT advantage for upright over inverted faces. These results indicate that individuals with an ASD may not be advantaged in inverted face recognition compared to non-ASD persons when only inner face features are presented. No significant between-group differences in attention to the eyes and mouth were identified.

141.059 59 Goal-Driven Vs. Mimetic Imitation in School Children with Typical Development and Autism Spectrum Disorders. L. Jimenez*¹, M. J. Lorda², B. Permuy¹ and C. Mendez¹, (1)University of Santiago, (2)Adapta Consultores

Background: Imitation is known to be affected in people with Autism Spectrum Disorders (ASD), but it remains unclear whether these problems should be taken as a primary deficit in autism, or whether they are a consequence of some other core deficits. This study started from Hamilton's (2008) proposal on the existence of two routes for imitation, and from her suggestion that a deficit in a mimetic route could account for the imitation pattern typically found in children with autism.

Objectives: Taking advantage of the end-state comfort (ESC) effect (Rosenbaum et al., 1990), which allowed us to model different action patterns fulfilling the same goals, but differing importantly in the efficiency of the observed action patterns, we designed a variant of the grasp imitation task reported in Hamilton et al. (2007), and analyzed whether a large group of children and adolescents with typical development (TD) emulated the goal, or reproduced the observed action patterns, even when they were not consistent with the ESC effect. We also tested a group of participants with high functional autism or Asperger syndrome, and analyzed their differences with respect to the control sample.

Methods: The task required participants to imitate the action of a model who grasped a wooden bar held horizontally over two cradles, and who grip it by inserting one of its two extremes on a metal pen holder. We manipulated the salience of the goal by using either a uniformly white bar, or a black-and-white bar, that made the goal of inserting one extreme of the bar in the container much more salient. The modeled grip (overhand vs. underhand) and the modeled end state (thumb down vs. thumb up) were also manipulated randomly between trials, to assess whether participants tended to emulate the goals, or to mimetically reproduce even the less functional modeled patterns.

Results: The results indicated that even the youngest children tested (7 to 9 years old) were affected by the ESC effect, and that participants with ASD also showed these planning effects. With age, participants with TD were progressively more prone to replicate even the less functional actions performed by the model. Participants with ASD emulated the observed goals to the same extent than did the control group, but they tended to imitate the specific actions less frequently when they ended in uncomfortable end states.

Conclusions: The results are consistent with the claim that participants with ASD are able to emulate the goals achieved by a model in an explicit imitation task, but that they show a delayed pattern of mimetic imitation, which is consistent with the dual-route model of imitation proposed in Hamilton (2008)

141.060 60 High Functioning Children with ASD Are Delayed in the Developmental Progression of Theory of Mind and in the Development of an Understanding of Teaching. J. Knutsen* and D. Frye, *University of Pennsylvania*

Background: The concept of teaching can be defined as an intentional activity to impart knowledge to another based on a perceived knowledge difference between teacher and learner. Typically developing (TD) preschool children develop an understanding of teaching that aligns with the development of theory of mind (ToM) (Woodburn, 2008; Ziv & Frye, 2004; Ziv, Solomon, & Frye, 2008). TD children's understanding of teaching as a function of mental states plays a critical role in their knowledge acquisition, social competence, and school readiness (e.g., Astington & Pelletier, 2005; Olson

& Bruner, 1996; Woodburn, 2008). In contrast, when and how children with Autism Spectrum Disorders (ASD) develop an understanding of teaching has not been examined and little research has investigated the specific sequence of their ToM development (Peterson, Wellman, & Liu, 2005; Peterson et al., 2012). Given that socio-cognitive impairment is a key characteristic of Autism, we hypothesize that children with ASD are impaired or delayed in their ToM development and in their development of an understanding of teaching.

Objectives: To investigate in high-functioning children with ASD (HFASD) the progression of ToM development and the understanding of the two core components that underlie the concept of teaching: (a) the knowledge difference between teacher and learner, and (b) that teaching is an intentional activity.

Methods: Participants were recruited through the Autism Instructional Methods Survey (AIMS) study (Mandell et al., 2010). Inclusion criteria for participation included verbal ability within the normal range (≥ 80), assessed using the Differential Ability Scales (DAS-II). Preliminary data are presented for 35 HFASD (32 boys, mean age 8:1, range 6:5-8:10) and 23 TD controls (20 boys, mean age 6:4, range 5:8-7:6) individually matched on verbal mental age. Children completed Wellman and Liu's (2004) ToM scale and an understanding of teaching scale (Woodburn, 2008). Control questions were included for all tasks in both measures.

Results: For the ToM scale (5 tasks), a group difference was found between HFASD and TD participants on both the knowledge acquisition task and false belief task, $p < .05$, respectively, Fisher's exact test. For the teaching scale (7 tasks), a group difference was found in the overall teaching score with HFASD performing worse than TDs ($t(50) = -2.63$, $p = .01$). On the individual tasks, a difference was found between target and control participants on the embedded teaching task, $p < .06$, Fisher's exact test. Data collection is ongoing and will include an overall sample of 70 participants (35 ASD, 35 TD).

Conclusions: These initial findings suggest that compared to their younger, verbal mental age-matched TD counterparts, children with HFASD

are delayed in ToM development and in developing an understanding of two core components that underlie the concept of teaching: (a) the knowledge difference between teacher and learner, and (b) that teaching is an intentional activity. Gaining knowledge about when and how children with ASD develop an understanding of teaching may provide information critical for learning and teaching in this population, and may also advance theories of social competence, moral reasoning, and academic development.

141.061 61 Impairments in Scene Construction Ability May Underlie Difficulties with Remembering the Past and Imagining the Future in People with Autism. S. E. Lind^{*1}, D. M. Williams¹, D. M. Bowler² and A. Peel¹, (1)*Durham University*, (2)*City University London*

Background:

There appears to be a common network of brain regions that underlie the ability to recall past personal experiences (episodic memory) and the ability to imagine possible future personal experiences (episodic future thinking). At the cognitive level, these abilities are thought to rely on "scene construction" (the ability to bind together multi-modal elements of a scene in mind -dependent on hippocampal functioning) and temporal "self-projection" (the ability to mentally project oneself through time - dependent on prefrontal cortex functioning).

Objectives:

Although ASD is characterised by diminished episodic memory, it is unclear whether episodic future thinking is correspondingly impaired. Moreover, the underlying basis of such impairments (difficulties with scene construction/self-projection/both) is yet to be established. The current study therefore aimed to elucidate these issues.

Methods:

Twenty-seven intellectually able adults with ASD and 29 age- and IQ-matched neurotypical comparison adults completed a version of a task developed by Hassabis and colleagues (2007). Participants were asked to describe (a) imagined atemporal, non-self-relevant fictitious scenes (fictitious scenes condition), (b) imagined

plausible self-relevant future episodes (episodic future thinking condition), and (c) recalled personally-experienced past episodes (episodic memory condition). Tests of narrative ability and theory of mind were also completed.

Results:

Performances of participants with ASD were significantly and equally diminished in each condition and, crucially, this diminution was independent of general narrative ability.

Conclusions:

Given that participants with ASD were impaired in the fictitious scene condition, which does not involve self-projection, we suggest the underlying difficulty with episodic memory/future thinking is one of scene construction.

141.062 62 Intact Face-Specific Adaptation in Autistic Adults. R. Brewer¹, R. Cook², P. Shah³ and G. Bird^{*4}, (1)*Birkbeck, University of London*, (2)*City University London*, (3)*Birkbeck College*, (4)*Birkbeck College, University of London*

Background: Reports of diminished facial aftereffects in autistic populations have been interpreted as evidence of deficient adaptive recalibration of face-specific representations. However, previous studies of facial adaptation in ASC populations have presented adapting and test stimuli at the same display location and at either the same or similar scales, thereby confounding face-specific and retinotopic adaptation. This raises the possibility that diminished aftereffects seen in autism reflect an absence of retinotopic adaptation, potentially due to atypical patterns of facial fixation, rather than deficient face-specific representations.

Objectives: The present study sought to determine whether ASC populations demonstrate reduced facial aftereffects when steps are taken to minimize the influence of low-level retinotopic adaptation, and guide participants' fixations when viewing the adapting stimuli.

Methods: Thirty-two participants completed expression and identity adaptation procedures; 16 with (15 males; mean age = 39.2 years) and 16 without (12 males; mean age = 32.6 years) a clinical diagnosis of ASC. To minimize the effects

of retinotopic adaptation, adapting and test stimuli were presented at different locations and were subject to a substantial scale disparity.

Results: Both the ASC and neurotypical groups demonstrated robust identity aftereffects, $M = 10.3\%$ ($SD = 7.7\%$) and $M = 11.9\%$ ($SD = 4.2\%$), respectively. The magnitude of the identity aftereffects did not differ between the groups, or correlate with autism severity, as indexed by either ASQ or ADOS score. Similarly, both the ASC and neurotypical groups demonstrated substantial expression aftereffects, $M = 6.8\%$ ($SD = 7.5\%$) and $M = 6.0\%$ ($SD = 6.6\%$), respectively, but no group difference emerged. Again, the magnitude of the expression aftereffects failed to correlate with either the ASQ or ADOS indices of autism severity.

Conclusions: Having adopted methods that reduce the contribution of retinotopic adaptation, we observed intact facial identity and expression aftereffects in adult participants with ASC. Crucially, these results argue against disturbed face-specific representation in ASC. Instead these data suggest that diminished aftereffects reported in ASC populations likely reflect reduced low-level retinotopic adaptation. In the absence of a fixation guide during the presentation of adapting stimuli, atypical patterns of gaze fixations may render ASC individuals less susceptible to the effects of retinotopic adaptation. Alternatively, ASC participants may fixate typically during adaptation, but show a genuine deficit of adaptation-induced calibration in retinotopic visual areas.

141.063 63 Is There an Overlap in the Domain of Theory of Mind Between Autism Spectrum Disorders and Schizophrenia Spectrum Disorders? Exploring Qualitative Differences. L. Boada^{*1}, G. Lahera² and M. Parellada³, (1)*Child and Adolescent Psychiatry Department, Hospital General Universitario Gregorio Marañón, Instituto de Investigación Sanitaria Gregorio Marañón, IISGM, CIBERSAM*, (2)*University of Alcalá*, (3)*Child and Adolescent Psychiatry Department, CIBERSAM, Instituto de Investigación Sanitaria Gregorio Marañón, IISGM, Hospital General Universitario Gregorio Marañón*

Background:

Several recent studies have demonstrated, in addition to genetic overlap (Carroll, 2009), a similarity between autism and schizophrenia in some psychological domains such as theory of

mind (ToM) (Spek, 2010). However, at a behavioral level, daily functioning and clinical impression make the two disorders quite different, and they are now considered independent disorders (DSM-IV-TR, ICD-10). At present, there is a dearth of instruments able to validly distinguish individuals with Asperger's syndrome from adults with schizophrenia that reflect these subtle differences in ToM. The Movie for the Assessment of Social Cognition (MASC) (Dziobek, 2006) is a promising social cognition instrument that may help differentiating mental state attribution in Asperger and schizophrenia patients. It evaluates ToM through video scripts of four characters interacting in a social situation, and it approximates social interactions as they actually happen in everyday life. Furthermore, it has shown good psychometric properties in English and in Spanish (Lahera, in preparation). In particular, compared with others, this instrument has a dimensional theoretical approach that operationalizes social cognition in a continuum: from mental state inferences that are "insufficient" to mental attributions that are "too-excessive," paralleling the hypothesis that states that "Psychosis and autism are diametrical disorders of the social brain (Crespi, 2008, 2010).

Objectives:

1. To evaluate ToM in Autism Spectrum Disorders and Schizophrenia Spectrum Disorders
2. To study qualitative ToM deficits in both disorders (undermentalization vs. overmentalization)
3. To study different psychometrics properties of four different-ToM-instruments in these two clinical-populations

Methods:

After being approved by the Institutional Review Board (IRB) of the Hospital Gregorio Marañón, Madrid, we recruited three groups of participants: twenty participants diagnosed with Asperger's syndrome and no comorbid disorder (DSM-IV-TR, ADOS-G, IQ > 85), twenty participants with schizophrenia (DSM-IV-TR, K-SADS, SCID-I) treated at Hospital Universitario Gregorio Marañón of Madrid, and twenty healthy volunteers from the

same area. In the three groups, the gender distribution was 5 women to 15 men, and the age range was 16-30 years. All groups were matched individually for age, gender, and years of education.

We administered the Frith-Happé animations (Abell, 2000; White, 2011), the Strange Stories (Happé, 1994), the Hinting Task (Corcoran, 1995) and the MASC (Dziobek, 2006) to each participant.

Hypotheses: We expect to find 1) that there is good correlation among the four instruments, with the MASC being the one that discriminates best between the two clinical groups; 2) Despite this, we expect that both clinical groups will be impaired in ToM attributions as measured by all the instruments; and that 3) MASC overmentalization errors will be significantly higher in the schizophrenia group while undermentalization errors will be significantly higher in the Asperger group, compared with the healthy-control-group.

Results:

We are currently finishing the evaluations. By May 2013, we will have the final results of the study of these four ToM instruments comparing young individuals with schizophrenia, Asperger's syndrome, and typical development.

Conclusions:

We expect to find that both groups of disorders have difficulties in tasks of theory of mind, with schizophrenia patients being particularly affected by overmentalization processes and Asperger Syndrome by undermentalization deficits.

141.064 64 Losing Face: Preschoolers with ASD Do Not Reference the Face When Decoding Intentional Actions. S. Paterson*¹, J. Parish-Morris², R. M. Golinkoff³, S. Kauper¹, R. Pulverman⁴ and K. Hirsh-Pasek⁵, (1)Children's Hospital of Philadelphia, (2)University of Pennsylvania, (3)University of Delaware, (4)Delaware State University, (5)Temple University

Background:

Understanding intentionality is important for daily social interactions and language comprehension.

This is particularly true for relational words like verbs (Behrend & Scofield, 2006) that carry the core meanings of sentences and for prepositions that describe relationships between two entities. Recent research suggests that children with ASD use fewer verbs and prepositions than typical children (Lopez & Lord, 2009). Given the link between intention understanding and language development, we suggest that clarifying the nature of intention understanding in ASD could lead to targeted language interventions that facilitate the acquisition of verbs and prepositions.

Objectives:

We explored intention understanding in children with ASD using an established paradigm (Baldwin et al. 2001). In the original study, infants were familiarized with videos of actors performing action sequences and tested with videos in which the action sequence was interrupted at various points. Increased looking at interrupted action sequences was interpreted as evidence that infants could parse continuous actions based on intention structure. In the present study, children watched the same videos and similar analyses were conducted. Given that children with ASD demonstrate abnormal attention to faces (McPartland et al., 2011), we also examined gaze fixations to the actor's face and looks to different aspects of the scene.

Methods:

Thirty-three 5-year-old children with ASD and 26 typically developing controls (matched on NVIQ) were familiarized with a video of a woman performing an intentional action sequence. At test, half the sample saw a video with a 1.5 second pause *before* the intention was completed, and half saw a video with a pause *after* the intention was completed. All individuals also saw control trials with a pause inserted once the intention was completed. The mean number of fixations and mean fixation duration was calculated for both the *full screen* and the *actor's face* using Tobii Software.

Results:

There were no significant differences in looking to the full screen or the actor's face between groups in the *after* condition. In the *before* condition, there was a significant effect of trial type: both groups looked more at the full screen in the *before* trials than in the control trials, $F(1,23)=5.92, p<.05$. When the mean fixation duration to the actor's face in each trial type was analyzed, there was a group by trial interaction, such that the ASD group looked longer at the face in the control trials, and the TD group looked longer at the face when the intention was not completed, $F(1,23)=5.48, p<.05$.

Conclusions:

Both groups looked longer at the full screen when an intentional action was interrupted, indicating that they understood basic intention structure. However only the typically developing children referenced the actor's face when the action was interrupted, perhaps attempting to glean information as to why the action was not completed. This pattern of referencing the face during interrupted actions was not present in the ASD group. These gaze data are currently being analyzed to examine the time course of these face referencing patterns and explore alternative looking patterns in the ASD group.

141.065 65 Metacognition and Theory of Mind in Adults with Autism Spectrum Disorder. C. S. Grainger*¹, D. M. Williams² and S. E. Lind², (1)Durham University, (2)Durham University

Background: It is widely acknowledged that Autism spectrum disorder (ASD) is characterised by impairments in understanding others' minds (theory of mind; ToM). Within the field there is much debate as to whether ToM and awareness of one's own mental states (metacognition) rely on the same underlying mechanism. However, little research has examined whether individuals with ASD also show diminished metacognitive ability. Accurate metacognitive judgements allow individuals to assess their current knowledge and tailor future learning accordingly. As such, impairments in metacognition could severely impact everyday functioning.

Objectives: Given the important role awareness of our own mind plays in adaptive functioning it is important to establish a metacognitive profile of ASD. As such this research aimed to assess metacognition in adults with ASD and employed

two tests typically used to assess awareness of one's own mind. Adults also completed a standard ToM task with the aim to examine whether impairments in ToM necessitate metacognitive impairments.

Methods: 10 participants with ASD and 10 age- and IQ-matched comparison participants completed a delayed judgement-of-learning (JOL) task and a feeling-of-knowing (FOK) task (data collection ongoing; final sample will be $n = 20$ per group). In the JOL tasks participants were asked to memorise 80 word pairs. After this learning phase participants were then presented with one word from each pair and asked to judge the likelihood that they would be able to *recall* the missing word when given a cued-recall test later. After all JOLs were made, the cued-recall task was administered immediately. For each participant a gamma correlation was calculated, to establish the accuracy of participants JOLs during the task. Participants also completed a standard feeling-of-knowing (FOK) task, during which they also memorised 80 word pairs. After learning the word pairs participants were presented with one word from the pair and asked to recall the missing word. For words participants failed to recall correctly, participants were then asked to judge the likelihood that they would *recognise* the missing word when presented with four options. In the last stage of this task participants were cued with one word from each pair and asked to select the missing word from four options. Gamma correlations were again calculated to establish the accuracy of participants' FOK judgments. Finally participants were asked to judge their performance on both tasks by self-reporting which task they thought they had correctly recalled more word pairs.

Results: Preliminary results suggest that individuals with ASD appeared to be significantly poorer at assessing their own mental states during the FOK task. Adults with ASD also found it difficult to accurately predict which of the two tasks they had performed better on. However, on the JOL task, individuals with ASD showed similar metacognitive ability to typically developing individuals.

Conclusions: The results suggest that, at least on some measures of metacognition, adults with ASD show metacognitive impairments. However

deficits do not appear to be absolute. These results are discussed in light of impaired ToM ability in the ASD group.

141.066 66 Movie for Assessment of Social Cognition (MASC):

Validation of the Spanish Version. G. Lahera^{*1}, L. Boada², E. Pousa³, I. Mirapeix⁴, G. Morón⁵, L. Marinas⁴, L. Gisbert⁶, M. Pamiàs⁶ and M. Parellada⁷, (1)*University of Alcalá*, (2)*Child and Adolescent Psychiatry Department, Hospital General Universitario Gregorio Marañón. Instituto de Investigación Sanitaria Gregorio Marañón. IISGM. CIBERSAM*, (3)*Salut Mental Parc Taulí, Parc Taulí. Sabadell. Hospital Universitari – UAB Universitat Autònoma de Barcelona*, (4)*Príncipe de Asturias University Hospital*, (5)*Child and Adolescent Psychiatry Department, Hospital General Universitario Gregorio Marañón. Instituto de Investigación Sanitaria Gregorio Marañón, IISGM, CIBERSAM*, (6)*Salut Mental Parc Taulí, Parc Taulí. Sabadell. Hospital Universitari – UAB Universitat Autònoma de Barcelona, Campus d'Excellència Internacional*, (7)*Child and Adolescent Psychiatry Department, Hospital General Universitario Gregorio Marañón. Instituto de Investigación Sanitaria Gregorio Marañón. IISGM. CIBERSAM*

Background: There is a need for proper characterization and standardized assessment of theory of mind and social information processing abilities that resemble, as much as possible, a "real world" integration of all these aspects. The Movie for the Assessment of Social Cognition (MASC) (Dziobek, 2006) was developed in 2006 and has been shown to have good psychometric properties and to be useful in social cognition research

Objectives: To translate, adapt, and validate a Spanish version of the MASC (MASC-SP) for use in patients with Asperger's syndrome and individuals with typical development, with the ultimate goal of facilitating its administration to the Spanish-speaking community.

Methods: Firstly, a transcription and translation of the English version of the MASC was made. After professional dubbing and subsequent editing of the audiovisual instrument, the MASC was administered to a sample of twenty-two patients diagnosed with Asperger's syndrome and twenty-six healthy volunteers. Other measures of social cognition were also administered: the Spanish version of the Strange Stories Task (Happé, 1994; Pousa, 2002), the Reading the Mind in the Eyes Test (Baron-Cohen et al., 2001a), and a basic facial emotion recognition task (Ekman & Friesen,

1971). We evaluated the MASC's psychometric properties with special emphasis on whether or not the adaptation affects the capacity to discriminate between healthy individuals and patients diagnosed with Asperger's syndrome. Twenty-two individuals diagnosed with Asperger's syndrome (DSM-IV-TR) were recruited (3 women and 19 men; mean age 21.94, SD 6.69, range 16-41). Twenty-six healthy volunteers were also enrolled (9 women and 17 men; mean age 22.92, SD 4.8, range 18-33), matching the experimental group with respect to age, gender, and years of education. In order to ensure the cognitive performance of patients with Asperger's syndrome, a brief scale for cognitive evaluation in psychiatric patients was administered (Screen for Cognitive Impairment in Psychiatry, SCIP; Purdon et al, 2005).

Results: The Asperger group scored lower on the MASC-SP (Mann-Whitney; $p = 0.000$), had fewer correct answers on the basic emotion recognition test (Mann-Whitney; $p = 0.000$), and poorer understanding of social situations per the Strange Stories Task (Mann-Whitney; $p = 0.000$) compared with the control group. The area under the ROC curves was 0.814 for the MASC-SP, 0.795 for the emotion recognition test, 0.912 for the Reading the Mind in the Eyes Test, and 0.806 for the Strange Stories Task. The Asperger group did not show cognitive deterioration and MASC-SP was proven to be independent for other general cognitive functions, as there was no significant correlation between MASC score and any of the SCIP subtests. Cronbach's alpha coefficient was 0.86, demonstrating satisfactory internal reliability (> 0.80) very similar to the original instrument (0.84).

Conclusions: The Spanish adaptation of the MASC can be a useful, ecologically valid tool for assessing social cognition.

141.067 67 Overimitation in Children with Autism Spectrum Conditions. L. E. Marsh*, D. Ropar and A. Hamilton, *University of Nottingham*

Background: Typically developing children frequently copy unnecessary actions with high fidelity, this is termed overimitation. The degree to which children overimitate seems to be socially modulated (Over & Carpenter, 2012). Children with autism have documented social difficulties and may also have an imitation deficit. Therefore,

it seems unlikely that children with autism will engage in overimitation. However, children with autism have previously been shown to faithfully imitate inefficient tool selection and use with novel objects (Nielsen & Hudry, 2010) but it is unclear whether this overimitation is due to social responsiveness in participants with autism or due to the causal reasoning demands which may confound the task.

Objectives: The present study tests whether children with autism spontaneously overimitate unnecessary actions when the causal reasoning demands of the overimitation task are reduced. In addition, the study also tests whether children with autism are able to explicitly differentiate necessary from unnecessary actions.

Methods: 27 children with autism, 27 chronologically age-matched (CA) and 27 verbal mental age-matched (VMA) controls took part. Each participant had the opportunity to overimitate on five trials. In each trial the participant watched a demonstrator complete a three step sequence of actions on a set of simple, familiar objects such as building a block tower or retrieving something from a plastic lunch box. Within each action sequence, two actions were necessary to achieve the goal and one was unnecessary. After viewing the demonstration, participants were instructed to complete the action goal as quickly as they could. Overimitation was recorded if the participant completed the unnecessary action. Following imitation, children were asked to rate how 'sensible' or how 'silly' each action in each sequence was.

Results: All children were able to complete the action goal. However, children with autism overimitated unnecessary actions significantly less than both the CA- ($p=0.001$) and VMA- ($p=0.02$) matched controls. Furthermore, children with autism were less able to differentiate sensible and silly actions when asked explicitly (CA: $p=0.0001$, VMA: $p=0.007$).

Conclusions: These results show that children with autism accurately copy goal directed actions but do not overimitate in circumstances where typical children do. This lack of overimitation means that children with autism miss out on a wealth of social learning opportunities that typical children exploit. Our data show an interesting dissociation between

implicit and explicit levels of measurement on the task. On one hand, children with autism implicitly understand the rationality of the demonstrated actions as they selectively imitate only the necessary actions. However, they are unable to explicitly distinguish 'sensible' from 'silly' actions. The consequences of these results for autism and for models of overimitation will be discussed.

141.068 68 Recognition and Expression of Emotions in Autism: Clinical Significance and Hierarchy of Difficulties Perceived by Parents and Experts. D. Lundqvist*¹, S. Berggren¹, H. O'Reilly², S. Fridenson³, S. Tal³, S. Newman⁴, O. Golan³, S. Baron-Cohen² and S. Bölte¹, (1)*Karolinska Institutet*, (2)*University of Cambridge*, (3)*Bar-Ilan University*, (4)*Comperia Ltd*

Background:

The recognition and expression of emotions is a challenge for children with Autism Spectrum Conditions (ASC). Thus, early training in these skills is important in order to achieve social inclusion. Within an EC-FP7-financed project ("ASC inclusion", www.asc-inclusion.eu), European partners are collaborating around the development of a computerized training tool for socio-emotional skills in children with ASC aged 5 to 10 years.

Objectives:

Children with ASC will learn when and how to recognize and express 20 different emotions (Afraid, Angry, Ashamed, Bored, Disappointed, Disgusted, Excited, Frustrated, Happy, Hurt, Interested, Jealous, Joking, Kind, Proud, Sad, Sneaky, Surprised, Unfriendly, Worried). The objective of this study was to explore and validate the choice of emotions using parent and expert ratings in different cultures.

Methods:

Three different surveys (S1, S2, S3) were run each in Sweden, the U.K. and Israel. [S1] assessed the perceived similarities and differences between the selected emotions in N= 716 typical adults. [S2] assessed the importance of the emotions and the degree of difficulty of these emotions in ASC judged by N = 88 parents of children with ASC aged 5 to 10 years. [S3] assessed the same issues as S2 but as judged by

47 ASC clinicians. Data from S1 was compiled to a similarity matrix and subjected to multi-dimensional scaling analyses (MDS), with the purpose of mapping between-emotion similarities, and to extract underlying emotional dimensions. In both S2 and S3, the relation between ratings of importance and difficulty was analysed. Likewise parents and experts ratings were compared. Data from S2 and S3 were related to the underlying dimensions of S1.

Results:

The selected 20 emotions rely on three main underlying dimensions; closely resembling Wundt's classical dimensions of valence, arousal and dominance. There was a close relationship between ratings on difficulty and clinical significance well as between parents' and experts' ratings. Emotions rated as easy by both parents and experts were also rated as of high significance, and vice versa ($r \approx .70$; $r^2 \approx .50$). The difficulty ratings of parents and experts were related to the emotional dimension of valence, demonstrating that, in particular for older children (aged 8 to 10 years) with a lower functioning level, negative emotions are more difficult to master than positive emotions.

Conclusions:

Results show that parents and experts strongly agree with regards to how they judge the difficulty and significance of emotional states for ASC children. The relationship between these ratings and an underlying valence dimension confirm earlier data showing larger difficulties with negatively than positively valenced emotions in ASC. Findings are valuable to validate the choice of emotions that will be taught to in ASC and will be applied to the development and sequencing of emotion tutorials for the ASC-Inclusion online training platform.

141.069 69 Reduced Perceptual Interactions Between Dynamic Facial Elements in Autism. R. Cook*¹, P. Shah² and G. Bird², (1)*City University London*, (2)*Birkbeck College*

Background: When neurotypical individuals view an upright face that repeatedly opens and closes its eyes, the presence of asynchronous mouth movements slows down the perceived velocity of the eyelids. However, when the same dynamic

facial stimuli are viewed upside-down, this illusory slowing is greatly diminished. This illusion is thought to result from perceptual predictions about eye movements derived from the direction of mouth movements. The process of reconciling these predictions with veridical sensory signals, gives rise to the illusory slowing. The absence of the effect when faces are inverted indicates that dynamic cross-feature predictions are orientation-specific, and accords with the literature on 'holistic' or 'configural' representation of upright static faces.

Objectives: In light of suggestions that individuals with autism show reduced ability to i) derive perceptual predictions and ii) represent faces holistically, the present study sought to determine whether they also show reduced susceptibility to the illusory slowing of eyelid transitions induced by asynchronous mouth movements.

Methods: We compared the performance of a group of adults with autism ($n=12$) and a group of age, IQ and gender matched neurotypical controls ($n=12$) on a psychophysical procedure designed to measure the perceived duration of eye-opening and eye-closing transitions, when viewed with an accompanying mouth movement with a phase difference of 90° . Upright and inverted trials were randomly interleaved, and separate psychometric functions estimated for the two conditions.

Results: As expected, the neurotypical controls showed a highly significant inversion effect, whereby the perceived duration of the eyelid transitions was greater when viewed in the upright orientation, than when viewed upside-down. In contrast, the autism group showed no evidence of the illusion whatsoever; they perceived the transitions of the eyelids to be of equivalent duration when face stimuli were viewed upright and inverted.

Conclusions: The present findings add support to previous claims that individuals with autism show a significantly reduced tendency to represent upright faces holistically and thereby derive cross-feature predictions. Crucially, these findings extend previous reports with static faces, by demonstrating atypical whole-face processing of dynamic stimuli.

141.070 70 Relationship Between Eye-Movement Patterns and Social Understanding in Children with an Autism Spectrum Disorder When Watching TV Soaps. K. Evers*¹, F. Hermens², J. Steyaert³, I. Noens¹ and J. Wagemans¹, (1)University of Leuven (KU Leuven), (2)University of Aberdeen, (3)Maastricht University Hospital

1. Background: It is no surprise that the research field on emotion perception in individuals with an Autism Spectrum Disorder (ASD) is immense, since social impairments form the core features in ASD. Despite mixed findings, most researchers using stimuli with a high ecological validity found evidence for impaired emotion processing in children with ASD. Furthermore, some perceptual symptoms seem to be related to social processing, including atypical eye-contact and difficulties in gaze following behavior. Investigating eye-movement patterns, most research has generally found atypical scanning patterns in ASD. However, not all studies provided evidence for major differences in viewing style, or they only found evidence for more subtle differences between children with and without ASD.

2. Objectives: Our aim was to investigate the relationship between eye-movement patterns and socio-emotional understanding in children with ASD, using ecologically valid stimuli.

3. Methods: Two groups of 6-to-10 year old children without intellectual disabilities ($IQ >= 70$), group-wise matched for age and intelligence level, participated: an ASD group ($N = 16$, 13 boys and 3 girls), with a diagnosis based upon a multidisciplinary assessment according to DSM-IV-TR criteria, and a typically developing (TD) group ($N = 26$, 22 boys and 4 girls), who scored below T70 on the Social Responsiveness Scale (SRS). Five episodes from a Dutch-spoken soap series for children were shown while eye-movements were recorded using an Eyelink 1000 system. Socio-emotional insight was measured with a questionnaire at the end of every episode, using five subtypes of questions: 1. Emotion recognition, 2. Emotion clarification, 3. Simple theory of mind, 4. Complex theory of mind, and 5. Visual details.

4. Results: When examining the global scanning parameters, no group differences were found between children with and without ASD in fixation count, fixation duration, or saccade amplitude. In

addition, when comparing fixations on four dynamic regions of interest (ROI; face, body, eyes, and mouth), we did not observe differences in viewing time on these ROIs for the video clips analyzed so far. However, children with ASD tended to perform worse on the social-emotional insight questions, especially on those questions concerning Emotion recognition and Emotion clarification, and tended to perform better on the questions concerning Visual details.

5. Conclusions: We compared viewing patterns of children with and without ASD when watching soap opera episodes. No evidence for differences in global scanning parameters was found. Preliminary results showed no differences in fixation times in face, body, eyes, or mouth. Future analyses could include more subtle scanning parameters, such as mouths of speaking and non-speaking persons, and alternations between socially interacting individuals.

Children with ASD tended to perform worse on the questions concerning social-emotional insight, which were asked at the end of every episode. Future analyses will compare the qualitative components of the answers in both participant groups. Besides, socio-emotional insight scores, as measured with our questions, will be correlated with eye-movement patterns. Moreover, we will investigate the relationship between socio-emotional insight in this experiment, and SRS scores.

141.071 71 Reputation Management: Evidence for Intact Ability but Reduced Propensity in Adults with Autism. E. Cage*¹, E. Pellicano², P. Shah¹ and G. Bird¹, (1)*Birkbeck College*, (2)*Centre for Research in Autism & Education*

Background:

People often change their behaviour when other people are around to protect their reputation. Previous research has shown that adults with autism fail to change their behaviour when being observed donating to charity, which the authors claimed to be due to fundamental problems in theory of mind (Izuma, Matsumoto, Camerer, and Adolphs, 2011).

Objectives:

The current study aimed to test an alternate explanation for this apparent lack of reputation management; that autistics find a good reputation less intrinsically rewarding. As such, there may be situations in which adults with autism are more likely to manage their reputation when it is rewarding for them to do so.

Methods:

Twenty typical and 19 autistic adults, matched for age and intellectual ability, donated to charity and to a person, both when alone and when observed by another person (a confederate). Critically, for half of the participants within each group, the observer was also the recipient of their donations and participants were told that the observer would subsequently have the opportunity to donate to them (motivation condition). This manipulation was designed to encourage a 'tit-for-tat' strategy in the participant and thus motivate reputation management in order to receive donations in return. The remaining participants were told that the person watching was simply observing the task's procedure (no motivation condition).

Results:

Results confirmed that autistic adults did not donate more to charity when observed. Importantly, both typical *and* autistic adults in the motivation condition donated significantly more to the person when watched by that person, presumably as there was a potential reward to be gained by doing so. Self-report data also suggested that the autistic participants were aware of the potential effect of their behaviour on the observer. Nevertheless, the motivation effect was significantly attenuated in the autistic individuals in comparison to the typical individuals.

Conclusions:

The results indicated, contrary to Izuma et al.'s (2012) claims, that autistic adults have the ability to manage their reputation in certain situations. The fact that they showed a reduced propensity to engage in reputation management under motivating conditions, however, suggests that motivational problems may precede social cognitive difficulties.

141.072 72 Self-Presentation in Children and Adolescents with High-Functioning ASD. A. M. Scheeren*¹, H. M. Koot¹ and S. Begeer², (1)VU University, (2)University of Sydney

Background:

A successful self-presentation requires an understanding of others' perspectives as well as motivation to convey a positive image of oneself. Children and adolescents with an autism spectrum disorder (ASD) are known to have difficulties adopting others' perspectives and also show a reduced social motivation. Therefore, the self-presentation skills of children and adolescents with ASD may be particularly impaired. Indeed, two previous small-scale studies indicated that children with ASD are less strategic in their self-presentation, that is, their self-presentation was less attuned to specific audience preferences (Begeer et al., 2008; Scheeren et al., 2010).

Objectives:

This is a first large-scale study to compare the self-presentation skills of children and adolescents with high-functioning ASD (HFASD) to those of typically developing (TD) peers.

Methods:

Ninety-six school-aged children and adolescents with HFASD and 56 TD peers (6-18 years) participated in this study. At the start of the interview each participant was asked to introduce him/herself to the interviewer (baseline condition). Later the participant was again asked to tell something about him/herself, but now the participant was told that the information would be used to select children for a prize-winning game (self-promotion condition). Number of strategic self-statements (i.e., self-statements emphasizing game-related abilities) was tallied in each condition. We used a fun-rating to estimate children's motivation to participate in a prize-winning game and a parent questionnaire (Social Responsiveness Scale) as a global index for the child's everyday social motivation and social cognition.

Results:

A MANOVA with Group (HFASD vs. TD) and Age (primary vs. secondary school) as between-subject variables, Condition (baseline vs. self-promotion) as a within-subject variable, and proportion of strategic self-statements as a dependent variable did not show a main effect of Group or Age, but did reveal a Condition effect: all participants used significantly more strategic self-statements in the self-promotion condition compared to the baseline condition. A Group x Age x Condition interaction effect was found. Post-hoc analyses showed that TD children and adolescents performed largely similarly in both conditions, yet within the HFASD group children increased significantly more in their strategic self-statements in the self-promotion condition compared to adolescents (Age x Condition effect). Also, there was a trend ($p = .06$) for adolescents with HFASD to increase less in strategic self-statements compared to TD age mates. Proportion of strategic self-statements was positively correlated with fun-ratings only in TD children ($r = .45$) and social motivation only in children with HFASD ($r = .45$), but was unrelated to children's social cognition.

Conclusions:

Intact strategic self-presentation of school-aged children with HFASD, but a reduced strategic self-presentation of adolescents with HFASD suggests that motivation, more so than social understanding (which matures with age), may play a crucial role in their self-presentation. Indeed, within the children's groups, we found positive associations between measures of motivation and the degree of strategic self-presentation. A lack of social motivation may be more characteristic for older than young children with HFASD.

141.073 73 Self-Projection in Autism Spectrum Disorders. J. J. Finnemann*¹, M. Brun¹, R. Benoit² and S. J. White¹, (1)University College London, (2)MRC Cognition and Brain Sciences Unit

Background:

Recent research suggests that there is a core network of frontal, temporal and parietal regions that supports various forms of mental self-projection (Buckner & Carroll, 2007). These include prospection (a simulation of the future), retrospection (a projection of the self into the

past), navigation (a mental projection into an alternative place) and mentalising (adoption of a different perspective). The fact that people with ASD are frequently reported to exhibit difficulties in all of those areas raises the question of whether the underlying causes could be found in the atypical functionality of the self-projection network.

Objectives:

The current study investigated the nature of two different forms of mental self-projection in ASD: prospection and mentalising. By virtue of investigating mentalising as well as prospective memory, we were also interested in exploring the possibility of bringing together several well-described aspects of the cognitive profile of ASD which previously have been accounted for within separate theoretical stances (i.e. the 'theory of mind' and 'executive dysfunction' accounts).

Methods:

To test this hypothesis we invited a group of adults with ASD (N=30) and a control group of typically-developed adults (N=30) to perform a variety of tasks assessing 'self' and 'other' processing and prospection. The groups were matched for age, gender and verbal and performance IQ. Both groups filled in the AQ and all ASD participants were assessed on the ADOS. Furthermore all participants were also administered a battery of well-established theory of mind tasks and an adaptation of the Strange Stories Test.

The first experimental task was based on a test of self-reference using trait adjectives (Benoit et al., 2010), which was presented as a self/similar-other/dissimilar-other paradigm. In the first phase of the experiment, participants were asked to make personality trait judgments for themselves, their best friend and the Queen of England. Subsequently they were again prompted with adjectives descriptive of personality traits and had to decide whether they had seen them in the corresponding condition in the first phase.

The second task was a temporal discounting task (Mitchell et al., 1999) designed to elicit individual

differences in the way the participants discounted future monetary rewards.

Results:

Whereas the control group replicated previous research suggesting superior performance for self-processing compared to tasks requiring a mental representation of a similar or dissimilar other, the ASD group showed a distinct impairment in the processing of a similar other. Furthermore the ASD group also exhibited a different pattern of performance on the temporal discounting task, with a tendency to be willing to wait longer for bigger rewards.

Conclusions:

Taken together this suggests that the extent to which thinking about others and the personal future is modelled on the self varies as a function of perceived self-similarity and furthermore that this mechanism is atypically recruited by individuals with ASD. Thus impaired self-projection may prove to be a useful cognitive model of autism, uniting previously distinct theories and predicting a set of specific cognitive deficits.

141.074 74 Sensitivity to Emotional Stimuli in Autism Spectrum Disorder: The Effect of Emotional Images On Time Perception. C. Jones^{*1}, S. B. Gaigg² and A. Lambrechts², (1)University of Essex, (2)City University London

Background:

Temporal judgments can be distorted by the emotional content of stimuli. In the temporal bisection task the duration of an emotionally expressive face is overestimated compared to a neutral facial expression (e.g. Droit-Volet et al., 2004). It is hypothesized that this effect is driven by stimulus-induced increases in arousal, which speed the rate of an 'internal clock' that meters time. To date, performance on this task has not been explored in individuals with autism spectrum disorder (ASD). If individuals with ASD show overestimation of emotional stimuli then it would suggest that their implicit responsiveness to emotional cues is intact. However, the absence of the effect would indicate an atypical response to emotion.

Objectives:

(1) To establish whether temporal judgements in individuals with ASD or those with a high degree of self-reported autistic traits are modulated by the emotional salience of stimuli. (2) To see whether such effects are specific to emotional facial expression or generalise to other emotional images.

Methods:

Study 1 tested 85 undergraduate students, who also completed the Autism Quotient (AQ) questionnaire (Baron-Cohen et al., 2001). Study 2 tested 20 adults with an ASD and 26 comparison participants, matched on age and IQ. Participants were presented with the classic time bisection task in which they learnt two reference durations, one 'short' (400 ms) and one 'long' (1600 ms). During the testing phase they were presented with a variety of stimuli of intermediate durations and had to classify them as either more similar to the short or the long references. In two conditions, temporal judgements were assessed for face stimuli (angry, happy, fearful and neutral faces) and a selection of natural images (snarling dog, puppy, spider and flower) that varied in emotional salience.

Results:

As expected, participants in Study 1 overestimated the duration of fearful and happy faces compared to the neutral face, and overestimated the duration of the snarling dog and puppy compared to the flower. However, these effects did not correlate with self-reported autistic traits. In Study 2 the group with ASD overestimated the duration of both the emotional face and natural images compared to neutral face and flower.

Conclusions:

Individuals with ASD and individuals from the general population both with low and high levels of autistic traits show an implicit response to emotional stimuli, which is manifest in the overestimation of duration. Further, this effect is found both for human faces and for images of the natural world. The data do not suggest a

fundamental insensitivity to the arousing content of either facial or natural images in ASD. These findings have implications for understanding how emotional stimuli are processed in ASD and for better delineating typical and atypical aspects of emotion processing in ASD.

141.075 75 Social and Non-Social Threat Detection in Autism Spectrum Disorders. W. Worsham*, M. J. Larson and M. South, *Brigham Young University*

Background: Previous research demonstrates that individuals with Autism Spectrum Disorders (ASD) are inhibited in processing social cues, including social threat (Krysko & Rutherford, 2009). For example, while participants with ASD detect threatening faces more quickly and accurately than friendly faces, they demonstrate overall slower response times and increased error rates relative to typical controls (Krysko & Rutherford, 2009). Other research has shown that individuals with ASD do not display a disadvantage when detecting non-social threat-related stimuli (South et al., 2008). We are not aware of previous research that directly compares the within-subjects relationship for response to social threat versus non-social threat in ASD.

Objectives: We explored whether adolescents with ASD have difficulties detecting threat in general, or whether adolescents with ASD are only disadvantaged when interpreting threat relating to socially salient stimuli. We hypothesized that adolescents with ASD will demonstrate decreased reaction time and error rates relative to typically-developing adolescents when viewing social threat-related stimuli. We also hypothesized that, when viewing non-threat-related stimuli with no social context, children with ASD will display intact performance relative to typically developing children.

Methods: Participants included 25 adolescents (3 females) ages 15-18 and diagnosed with an ASD (ASD group); compared to 25 typically-developing controls (CON group, 4 females) matched on age (M = 17.24 years) and IQ (mean = 107). We utilized a "dot probe" task using words with either positive or neutral valence and both social threat ("lonely," "foolish," and "hopeless") and physical threat ("injury," "hazard," and "disease") words. The task displayed a word from one of the four categories, for 600 milliseconds prior to a dot appearing on the top or bottom of the computer

screen (Keogh, Dillon, Georgiou & Hunt, 2001). The participant was asked to respond as quickly and accurately as possible regarding the location of the dot, along with determining when the dot appeared on the screen.

Results: Accuracy for all categories was at ceiling (>97% for all conditions for both groups). Repeated measures ANOVA of response times for the combined groups showed no significant main effect for threat condition but did show a significant main effect for diagnostic group, with the ASD group significantly slower than controls. The group x threat condition interaction was statistically significant. Planned decompositions showed that, as hypothesized, the ASD group did show a significant main effect for threat condition [$F(2,23)=3.1, p<.05, \eta^2=.14$], with the Social Threat condition showing slower response time than the other conditions. There was no such effect for the TYP group as response time to all conditions was quite similar.

Conclusions: As hypothesized, adolescents with ASD displayed decreased reaction time to the social threat condition relative to the control group. However, there was no significant difference between groups in reaction time to the non-social threat condition. These results suggest that impaired threat detection in individuals with ASD is specific to social threat conditions rather than an overall delayed response to threat.

141.076 76 Social-Communicatively Cued Versus Goal-Directed Intention Understanding in Children with ASD. N. I. Berger* and B. Ingersoll, *Michigan State University*

Background: Intention is one of the earliest mental states to be understood in the typical course of development. Understanding intention is classically measured by imitation tasks that clearly separate the actor's goal from the outcome. A number of studies using modified versions of Meltzoff's (1995) unfulfilled intentions paradigm with children with autism spectrum disorders (ASD) have suggested that these children do not have a deficit in intention understanding. These sorts of findings would appear to indicate that children with ASD do not have a deficit in intention understanding despite showing significant impairments in related skills (e.g., imitation, imitation recognition, joint attention). There are, however, contradictory findings suggesting that children with ASD may

have some difficulty understanding intention - particularly when intention is conveyed using social-communicative cues, rather than goal-directed actions on objects. Considered together, the literature is equivocal in regard to the ability of children with ASD to understand intention.

Objectives: This study sought to examine performance across two measures of intention understanding (one goal-directed intention task and one social-communicatively cued intention task) in typically developing children and children with ASD. We also explored whether various assessment variables correlated with performance on measures of intention understanding.

Methods: The sample included 15 TD children and 15 children with ASD. Typically developing children were between the ages of 16 and 30 months old and were matched to ASD participants based on both developmental age and language age. Each child participated in two intention different tasks, one of which assessed understanding of intention by attending to actions on objects and the other of which necessitated attending to social-communicative cues to derive intention. Participants were also administered standardized measures of joint attention and imitation; imitation recognition was coded during periods of contingent imitation built into an unstructured imitation task.

Results: Relative to matched controls, children with ASD did not appear to exhibit deficits in understanding goal-directed intention as measured in an unfulfilled intention task. However, when required to attend to social-communicative cues to infer intention, children with ASD demonstrated impairment relative to typical controls. Preliminary analyses suggest that for children with ASD, greater intention understanding in the social-communicatively cued paradigm is positively related to frequency of initiations of joint attention and imitation recognition.

Conclusions: These results replicate previous work suggesting that children with ASD are not impaired in understanding other's intention when employing an unfulfilled intention paradigm. However, intention understanding deficits emerge in this population when children must rely on social-communicative cues. Problems utilizing

social-communicative cues to ascribe intention to the actions of others may be related to the difficulties in joint attention and imitation recognition observed in children with ASD.

141.077 77 Spanish Validation of A New and Advanced Test of Theory of Mind: Kaland's Stories From Everyday Life. O. Puig Navarro^{*1}, S. Lera Miguel², M. J. Rosa³, J. Castro-Fornieles², N. Kaland⁴ and R. Calvo Escalona², (1)*SGR 1119*, (2)*Hospital Clinic of Barcelona*, (3)*Fundació Clínic per la Recerca Biomèdica*, (4)*Lillehammer University College*

Background: One of the most salient characteristics of Autism Spectrum Disorders (ASD) is their failing to attribute mental states to themselves and others. There are some useful instruments to assess Theory of Mind (ToM) (Abell, 2000; Baron-Cohen, 1997) but often subjects with high functioning ASD (HF-ASD) find easy to pass second-order tasks. Among the most recent instruments developed to evaluate "advanced" ToM tasks there is the *Kaland's Stories from Everyday Life (SEL)* test (Kaland, 2002). This battery includes the ToM elements in a naturalistic story context. Children and adolescents with Asperger Syndrome performed worse than their matched controls to impute mental states in this test and needed more prompt questions and required more time to complete the tasks (Kaland, 2002, 2007).

Objectives: To validate a brief version of the *SEL* in a Spanish sample of HF-ASD children and adolescents and to compare with a group of healthy comparison controls (HC).

Methods: Participants were 27 HF-ASD participants (mean age=12.23±2.8) and HC (mean age=13.75±2.89) males. All patients fulfilled ASD criteria on DSM-IV. Exclusion criteria included an IQ<70, an active psychopathological condition and severe neurological or medical disorders. The *SEL* were translated into Spanish, it were back-translated into English and received the approval of the author. The research team systematized the scoring procedures and wrote a manual with the administration and scoring instructions. The evaluator read the 13 different types' stories and formulate control questions to check the verbal comprehension and two central questions to test participants' ability to infer physical (PI) and mental states (MI) from the story context. Prompt questions (PQ) were given if an incomplete answer was provided. The reaction

time was recorded before (RT) and after all prompt questions (RT_{PQ}). There was a second evaluator who was blind to the status of the subjects. Measures of verbal IQ and severity of ASD symptoms were registered.

Results: Internal consistency and inter-rater reliability were moderate to high (.60-.90). After covariation for verbal IQ, only the correlation between SCQ and MI emerged ($r = -.30$, $p = .05$), indicating that children with high levels of ASD symptoms kept on showing difficulties to infer the mental states in spite of a good verbal competence. PI and MI scores correctly classified 64% ($p = .015$) to 67% ($p = .021$) of participants in patients versus control group. When HF-ASD and HC compared controlling for verbal IQ, significant differences emerged in total PI ($t = -3.1$, $p = .004$) and MI ($t = -2.56$, $p = .014$) raw scores. This result indicated that the higher difficulties of HF-ASD in inferring physical and mental states were not only explicated by their verbal competence but by the clinical diagnostic.

Conclusions: In our Spanish sample, the *SEL* instrument showed adequate psychometric characteristics and includes an administration manual. Differences between groups were obtained in PI and MI. Children with more severe ASD symptoms kept on showing more difficulties to infer the mental states in spite of a good verbal competence. These preliminary findings suggest that the *SEL* is useful to evaluate ToM in HF-ASD children and adolescents.

141.078 78 Testing Sensitivity to Emotional Prosody in Minimally-Verbal LFA. J. Chiew¹ and M. M. Kjelgaard^{*2}, (1)*Beth Israel Deaconess Medical Center and Harvard Medical School*, (2)*MGH Institute of Health Professions*

Background:

Autism spectrum disorders (ASDs) are characterized by immense heterogeneity – from individuals with high-functioning autism (HFA) who demonstrate only limited deficits in social communication, to those who are low-functioning (LFA) and fail to develop any shared symbolic system of communication. It has been posited that typical infants utilize "prosodic bootstrapping" to acquire vocabulary and develop oral language: Child-directed speech presents infants with a unique affective speech register that cues them to distinguish individual speech sounds in their

native language. Yet research has found that very young children with ASD are less responsive to their mother's voice, which may hinder successful language acquisition. Perhaps the ability to perceive affective prosody is at the core of language and communication difficulties in the minimally verbal LFA subgroup, approximately 30% of the ASD population. While recent scientific inquiry has made gains regarding ASDs, little research examining the minimally verbal LFA subgroup has been undertaken to date. The present study sought to fill this gap, through an investigation of the ability of children on the autism spectrum, including minimally verbal LFA, to perceive angry, neutral, and happy prosody in low-pass filtered speech when provided with a structured training paradigm.

Objectives:

The main objective of this study was to determine the ability of children with ASD, including those who are minimally verbal, to perceive affective prosody. Secondly, this study also sought to determine what relationships exist between the ability to perceive affective prosody and social responsiveness and/or nonverbal cognitive ability.

Methods:

To date, 13 children with ASD (11 LFA, 2 HFA) and 21 neuro-typical (NT) children have completed the experimental task and two additional measures (nonverbal cognitive ability, social responsiveness deficits) for regression analyses. An innovative study design was developed that allowed minimally verbal LFA children to participate in and complete the experiment. First, low-pass filtered sentences were used to eliminate the confounding factors in linguistic stimuli that are associated with language abilities (e.g., knowledge of vocabulary, syntax), and to accommodate the heterogeneity within the autism spectrum. Second, a systematically scaffolded training paradigm was used to teach task expectations to all participants, supporting successful task completion.

Results:

ASD participants recognized prosodic conditions significantly less accurately than NT participants,

and took significantly longer times to recognize all sentences compared to NT participants. The NT group required a significantly longer time to recognize affective prosody in shorter sentences compared to longer sentences, while the ASD group showed no such sentence length differences. Angry prosody was consistently the most difficult to recognize across groups. Nonverbal cognitive ability was a significant predictor for successful recognition of neutral and happy prosody; although low nonverbal cognitive skills do not preclude minimally verbal LFA children from correctly perceiving affective prosody.

Conclusions:

This study demonstrated that it is possible for minimally verbal LFA children to successfully participate in experimental research using judgment tasks when provided with appropriate training, which is encouraging for translational purposes. Results pertinent to the HFA and minimally verbal LFA subgroups and the implications for intervention will be discussed.

141.079 79 The Influence of Typical Siblings On the Social-Communicative Behaviour and Theory of Mind Development in Children with Autism. K. A. O'Brien*, V. P. Slaughter and C. C. Peterson, *The University of Queensland*

Background: Research indicates that having siblings is positively associated with theory of mind (ToM) in typically developing (TD) children. Initially older but not younger siblings were found to facilitate ToM development (Ruffman et al., 1998) but when only child aged siblings (12 months to twelve years) were involved younger siblings also showed superior ToM skills to only children (Peterson, 2000). Social and communication impairments are core features of autism and ToM is also usually severely delayed. We previously found that although there was a small advantage in having a younger sibling, having an older sibling was a disadvantage for ToM development in children with ASD (O'Brien, Slaughter & Peterson, 2011) but no research has directly observed siblings playing together to explore the extent to which siblings of children with autism engage in interactions likely to facilitate ToM. **Objectives:** We conducted the present study to directly examine how the presence of older and younger siblings is associated with ToM development and intentional

communication by observing social-communicative behaviour and the different roles and forms and functions ASD children take when playing with older sibs compared with younger sibs. **Methods:** Participants were 24 dyads (12 older sibs and 12 younger sibs) of a child with an ASD (mean age=7.45 *SD*=2.50) and a child aged TD sibling (mean age=8.12 *SD*=3.99). The siblings were screened with the SCQ to rule out ASDs. All children completed a standard battery of ToM tasks, and the PPVT-III. ASD children were also assessed with the ADOS and VABS-II. Each sibling dyad played for 10 minutes in a free play session which was video-taped and coded using the coding scheme from the modified-classroom observation schedule (M-COSMIC) which was created to measure intentional communication (Clifford et al., 2010). **Results:** ToM and VMA were significantly better in ASD sibs with younger sibs compared with older sibs. ASD children in younger sibling dyads showed significantly more communicative-social behaviours than in older sibling dyads. A non-parametric (spearman) correlation found ToM was significantly correlated ($p < .01$) with age and VMA as well as the M-COSMIC categories of showing off/attention, shared attention, initiation and use of three word plus phases and negatively correlated with non-interaction/no response. **Conclusions:** Younger TD siblings of children with autism confer a benefit in ToM development and intentional communication. It is possible older siblings over compensate for their ASD sibling which may limit the effect of ToM development and the social learning of the ASD children. These finding could be used to create interventions involving siblings to improve theory of mind and intentional communication in ASD children. It may involve promoting play with younger siblings and teaching older siblings to not compensate for their ASD siblings.

141.080 80 The Relationship Between Fantasy and Empathy Among Young Adults with Autism Spectrum Disorders. M. K. Kalies*¹, M. M. Wasserman², R. Ellingsen³, J. Hopkins¹ and E. Laugeson⁴, (1)UCLA PEERS Clinic, (2)Pepperdine University, (3)University of California Los Angeles, (4)UCLA Semel Institute for Neuroscience & Human Behavior

Background: Empathy involves the capacity to recognize, identify, understand, and experience the emotional states of others, and is essential to the development and maintenance of meaningful relationships. Baron-Cohen and Wheelwright

(2004) found that those with Autism Spectrum Disorders (ASD) exhibit less empathy than typically developing individuals. Several factors may be associated with one's ability to empathize. In particular, the capacity to fantasize, a form of perspective taking, may be related to empathic ability. For example, Niec and Russ (1996) found that neurotypical children who are better able to engage in fantasy play exhibit greater empathy. While anecdotal reports suggest that many individuals on the autism spectrum, including young adults, participate in fantasy role-playing games (RPGs), the relationship between fantasy and empathy for those with ASD has yet to be examined to our knowledge.

Objectives: This study seeks to examine the relationship between self-reported fantasy and empathy for young adults with ASD. It hypothesized that young adults reporting greater fantasy will demonstrate greater empathic abilities.

Methods: Thirty-one young adults ranging from 18-27 years of age ($M=20.42$, $SD=2.109$) presenting for social skills treatment through the UCLA PEERS[®] for Young Adults Program participated in the study. Subjects completed baseline measures of empathy prior to treatment including the Empathy Quotient (EQ; Baron-Cohen & Wheelwright, 2004) and the Interpersonal Reactivity Index (IRI; Davis, 1983). In order to understand the relationship between fantasy and empathy, baseline self-reports on the IRI Fantasy Scale, which measures the tendency to imaginatively transpose oneself into fictional situations, were correlated with the EQ subscales of Cognitive Empathy Emotional Reactivity, and Social Skills using Pearson Correlations.

Results: Preliminary results reveal that higher self-reported baseline Fantasy Subscale scores on the IRI are significantly correlated with higher self-reported baseline Emotional Reactivity Subscale scores on the EQ ($p < .05$), which measures personal reactions to others' mental states. No correlations between the EQ subscales of Cognitive Empathy and Social Skills were observed with the IRI Fantasy Subscale scores.

Conclusions: Preliminary findings suggest support for the original hypothesis in that young adults who self-report greater use of fantasy also exhibit

greater empathy through their personal reactions to the mental states of others. These findings are important in that they suggest that those who engage in greater fantasy, perhaps through involvement in activities like live action role-playing (LARPing) or fantasy role-playing games (RPG) like Dungeons and Dragons®, may exhibit greater empathic abilities, thus, potentially fostering more meaningful interpersonal relationships.

141.081 81 The Relationship Between Autistic Traits, Depressed Mood and Social Problem-Solving. S. Jackson* and B. Dritschel, *University of St Andrews*

Background:

Previous research has established that Autism Spectrum Disorders (ASD) are associated with a high prevalence of depression and deficits in social problem solving. Poor social problem solving skills have consistently been shown to be a strong predictor of depression in numerous studies. There is evidence that individuals with subclinical levels of autistic traits also experience difficulties with depression. Only one study has previously examined the relationship between autistic traits, depressed mood and social problem-solving, but solely measured the process component of social problem-solving and failed to report on the subscale relationships of their measured variables.

Objectives:

This study examined if: (i.) higher levels of autistic traits are associated with higher levels of depressed mood; (ii.) higher levels of autistic traits are associated with deficits in social problem solving abilities (both process and outcome measures of social problem-solving); (iii.) social problem solving deficits are associated with higher levels of depressed mood; (iv.) social problem solving abilities play a mediating role in the relationship between levels of autistic traits and depressed mood; and (v.) how specific sub-components of social problem-solving (e.g., impulsivity, negative problem orientation) are associated with autistic traits and depressed mood; and, likewise, how sub-components of the autistic trait measure (e.g. attention to detail, imagination) are associated with depressed mood and social problem-solving ability.

Methods:

Seventy-seven university students completed four self-report measures: the Autistic Spectrum Quotient (AQ), the Beck Depression Inventory- II, the Social Problem Solving Inventory - Revised (process measure), Means-Ends Problem-Solving Test (outcome measure)

Results:

- Higher BDI-II scores were significantly associated with higher AQ scores ($r = .343$, $p < .002$), as well as three of the five AQ subscales.

- Higher AQ scores were significantly associated with poorer overall SPSP-R scores ($r = -.319$, $p < .002$), and overall MEPS score ($r = -.278$, $p < .01$). AQ scores were also significantly correlated with two of the five SPSP-R subcategories, while the combined effect of the SPSP-R and MEPS scores were significantly correlated four of the five AQ subscales AQ.

- Higher BDI-II scores were significantly associated with poorer overall SPSP-R score ($r = -.490$, $p < .002$), and overall MEPS score ($r = -.345$, $p < .002$).

- When the ability of social problem solving skills to predict depressed mood was controlled for, levels of autistic traits were no longer a significant predictor of levels of depressed mood ($p = .138$).

Conclusions:

Like individuals diagnosed with ASD, individuals displaying subclinical levels of autistic traits have difficulties with depressed mood and social problem-solving. Individuals with high levels of autistic traits are inclined to assume a negative orientation, express limited initiative to confront, and produce ineffective solutions when faced with social conflict scenarios. As social problem solving mediates the relationship between autistic traits and depressed mood, future work should examine the ability to develop positive and functional social problem-solving abilities in individuals with subclinical levels of autistic traits for the treatment of depressed mood.

141.082 82 The Validity and Scalability of the Five-Item Theory of Mind Scale for Use with Toddlers and Pre-Schoolers. N. Weber*, R. Hiller and R. L. Young, *Flinders University*

Background: The theory of mind literature has had a significant impact in the field of developmental psychology. Most notable is the link between this cognitive construct and typical social development, making theory of mind a key cognitive deficit in autism spectrum disorder (Hughes & Leekam, 2004). Despite its potential importance for typical development, two key issues affect our ability to draw conclusions from the extensive theory of mind literature. One is the continued focus on false-belief as the sole measure of theory of mind, despite this ability not emerging until around four years of age. The second is the lack of empirically validated measures of theory of mind, particularly outside false-belief tasks. These are two challenges that also currently limit our ability to accurately identify potential early theory of mind deficits (before the age one would expect false-belief understanding to exist).

Objectives: Wellman and Liu (2004) proposed a five-item scale said to assess first-order theory of mind development in the pre-school years. While this scale has shown promise in allowing the longitudinal assessment of early theory of mind development, it is yet to be used with children younger than 3.5 years of age. Our research aimed to assess the suitability of this scale for use with children from two years of age. Further to this we assessed the scalability of these five tasks with this younger age range, along with the tools validity against the oft-used Sally-Anne false-belief task.

Methods: Sixty-eight typically-developing pre-school children (ranging in age from 24 to 61 months) were assessed using the Australian version of the five-item theory of mind scale (Peterson, Wellman, & Liu, 2005), as well as a sixth Sally-Anne false-belief task. Abilities measured by the five-item scale are (1) diverse desires, (2) diverse beliefs, (3) knowledge access, (4) false belief, and (5) hidden emotion.

Results: All children showed comprehension of the control question presented in the first task, while the vast majority also showed comprehension of the presented scenarios for tasks two and three.

There was also evidence of children showing an understanding of diverse desires and diverse beliefs from two years of age. However, our data failed to replicate the strict scalability of these five tasks both overall and with only the older (over 42 months) or younger (under 42 months) age groups. Despite this, the tool showed good internal consistency and convergent validity against the Sally-Anne false belief task ($r = .67, p < .001$).

Conclusions: Our results provide initial evidence in support for the usability of this tool as a valid assessment of theory of mind for children from two years of age. However, based on our results we propose that the most accurate ability index should be based on the *total* items scored correct, rather than the currently used *highest* item scored correct. Results have clear implications for the ability for research to now empirically establish at what age a theory of mind deficit may be considered problematic, thus potentially paving the way for the early identification of this cognitive deficit.

141.083 83 Theory of Mind and Underlying Cognitive Mechanisms in Children with an Extra X Chromosome. S. Van Rijn*, *Leiden University, Leiden*

Background:

Approximately 1 in 700-1000 boys are born with an extra X chromosome, also known as Klinefelter syndrome (KS). Because of the risk for development of autistic symptoms, it has been suggested that studying individuals with KS may help in the search for cognitive, neural and genetic mechanisms underlying autism symptoms. In order to gain more insight in the gene-brain-behavior relations, it is important to dissect neurocognitive dysfunctions that mediate between the genetic level and the behavioral level.

Objectives:

The present study focuses on theory of mind skills, and underlying cognitive mechanisms, in children with an extra X chromosome.

Methods:

In total, 60 children (35 boys and 25 girls) with an extra X chromosome, 60 boys and girls with

ASD and 110 non-clinical controls participated in the study. The age range was 9 to 18 years. We used the Social Cognitive Skills Test (SCVT) to assess Theory of Mind skills. This test consists of 7 cartoon stories, with 8 questions for each story covering various levels of theory of mind complexity. The study also included a neurocognitive test battery assessing language skills, executive functioning and intellectual functioning.

Results:

Theory of mind scores were lower in the group with an extra X chromosome as compared to controls, and scores could not be differentiated from those in children with ASD. In the extra X group, 57 % of the children scored within the atypical range (below the 15th percentile). Performance was similar in boys and girls with an extra X. Regression analysis showed that theory of mind performance was significantly predicted by executive functioning (inhibition, fluency, attention, working memory, mental flexibility), but not by language skills or intellectual functioning.

Conclusions:

Our findings suggest that impaired theory of mind might help explain increased vulnerability for autism symptoms in children with an extra X. Executive dysfunctioning seems to play a crucial role in deficiencies in theory of mind. This knowledge may help in diagnosis and treatment of children with an extra X. The absence of gender effects is not only relevant for clinical practice, but may also provide important clues with regard to role of the extra X chromosome in cognitive development and related risk for autism traits.

141.084 84 Thinking about What Isn't True: Influences of Context, Processing Style and Emotional State On Reasoning Among Children with Autism. R. McKenzie*, *Plymouth University*

Background: The evidence for the ability of children with autism to reason about what is not true in real life is mixed. For example, Scott, Baron-Cohen and Leslie (1999) claim that children with autism can reason with content that is contrary-to-fact, whereas Leevers and Harris (2000) found performance on similar problems was at chance levels. This study seeks to address

this question by presenting contrary-to-fact and counterfactual problems with everyday content to children with autism. Previous mixed findings suggest that children with autism may be able to reason with contrary-to fact problems in certain cases, but not others. Children with autism are known to commonly experience negative affect and to be detail-based in their thinking style. Both of these factors have been shown to influence reasoning performance. We, therefore, explore whether children with autism can reason with contrary-to-fact and counterfactual material and the influence of contextual information, detail-based processing style and emotional state on their performance.

Objectives:

- To establish whether children with autism can reason with empirically false material
- To investigate the influence of context, processing style and emotional state on reasoning performance

Methods: 25 children between the ages of 7 and 16 years with high-functioning autism and 25 control children, matched on age, gender and IQ, took part in the study. The children were presented with contrary-to-fact and counterfactual reasoning problems, either embedded in a story context, or with basic instructions. Children were also given a measure of affect (The positive and Negative Affect Scale) and a measure of detail based processing (the Embedded Figures Task)

Results: Initial results suggest that children with autism are able to reason with empirically false material, but the typical facilitation of story context is not present. Emotional state has no significant bearing on reasoning performance. Detail-based processing is related to the ability to take account of context.

Conclusions: Children with autism are able to apply given rules when thinking about statements that are not empirically true. For the typical population the use of a fictional context is widely used to support this kind of thinking. Such approaches are not beneficial for all children with autism. For children with autism, the usefulness of using fictional scenarios to support reasoning with empirically false material may depend on their

individual processing style. These findings have important implications for educational practice.

Leevers, H. J. & Harris, P. L. (2000) Counterfactual Syllogistic Reasoning in Normal 4-Year-Olds, Children with Learning Disabilities, and children with Autism. *Journal of Experimental Child Psychology*, 76, 64-87.

Scott, F. J., Baron-Cohen, S. & Leslie, A. (1999) 'If pigs could fly': A test of counterfactual reasoning and pretence in children with autism. *British Journal of Developmental Psychology*, 17, 349-362.

141.085 85 Understanding Other People: Theory of Mind in Toddlers and Preschoolers with Autism Spectrum Disorder. E. Broekhof*, K. A. Bruidegom¹, L. Ketelaar¹, L. Stockmann² and C. Rieffe¹, (1)*Leiden University*, (2)*Centrum Autisme Rivierduinen*

Background: Theory of Mind (ToM) refers to the ability to understand the subjectivity of people's intentions, desires and beliefs. Research has shown that the development of this capacity is significantly delayed in children with an autism spectrum disorder (ASD). These studies have mainly focused on false belief understanding, while ToM is grounded on three fundamental mental concepts: intentions, desires and beliefs, which develop in a fixed order in TD children. Especially knowledge concerning intention understanding in children with ASD is limited. Moreover, to date, little research in this domain has included toddlers and preschoolers with ASD.

Objectives: The purpose of this study was to assess separate aspects of ToM functioning in young children with ASD compared with typically developing (TD) peers in order to gain more insight into ToM development in children with ASD.

Methods: The study included 139 children (66 with ASD, 73 TD, 21-72 months). A broad range of low-verbal-demand tasks were administered to measure various aspects of intention, desire and belief understanding.

Results: The outcomes showed that children with ASD understood two aspects of other people's intentions to the same extent as TD children. Yet, children with ASD scored significantly lower than

TD children on imperative comprehension; the ability to understand that someone intends to direct their attention in order to request an object. In addition, the ASD group scored lower on a desire task in which the protagonist preferred undesirable food items. No significant differences were found between both groups on false belief understanding.

Conclusions: Compared with the TD group, children with ASD did not show a delay in the first stage of ToM development: understanding other people's intentions, except for imperative comprehension. Yet, this involves responding to the other person's desire, which includes a motivational component. Additionally, children with ASD showed difficulties in acknowledging the subjective character of desires in an uncommon desire task. These outcomes indicate that a delay in ToM development is already present in toddlers and preschoolers. The absence of a difference in false belief understanding seems to contradict this. However, this finding could be explained by the young age of the samples; both groups had low scores on these tasks because belief understanding is still very much in development.

141.086 86 Using Visual Adaptation to Explore Facial Emotion Expression Representation in Relation to Autism Traits. P. C. Griffiths*, C. Ashwin and M. Brosnan, *University of Bath*

Background:

Autism spectrum conditions (ASC) are characterised by social-emotional difficulties, such as problems identifying and understanding the emotional state of others. Research investigating emotion processing in ASC has provided mixed results to date. However, a number of studies have shown people with ASC have deficits processing negative basic emotions on both a behavioural and neural level, with intact processing of positive or neutral emotions.

Visual adaptation is a paradigm where participants constantly view a stimulus for a period of time. This then alters the neuronal firing associated with coding for that stimulus and, thus, alters subsequent perception of that stimulus. The alterations in perception are typically a deviation from the adapting stimuli in the opposite direction. For example, adaptation studies with basic emotions have shown that visually adapting to an emotion of one valence (e.g. negative)

results in perceiving a neutral face as displaying the opposite valence (e.g. positive). This method can be used to probe underlying neural representations of the visual-perceptual world.

Objectives:

The current study investigated emotion processing differences related to autism using a visual adaptation paradigm. As autism is a spectrum condition, it is hypothesised that emotion processing deficits would be evident in subclinical individuals with a high degree of autism traits.

Methods:

94 participants from the general population were recruited and assessed for the number of autism traits they possess using the Autism-Spectrum Quotient (AQ). Participants were assigned to either a 'high' or 'low' autism trait group based on their AQ scores, and basic emotion recognition ability was assessed. Participants then completed a visual adaptation task with images displaying basic emotions and anti-emotions created to be their perceptual. During adaptation, participants viewed an emotional expression for 30s before making a judgement regarding the expression shown on a briefly presented neutral expression test face. We expected those with high autism traits to show reduced adaptation effects compared to those with low autism traits when the perceptual after-effect involved a negative emotion representation, but no group differences when the after-effect involved positive emotions.

Results:

Results showed an interaction between Autism Trait Group and Adapting Emotion ($F(1,92) = 5.25, p < .05$). This was further explored to show that high autism trait participants had more difficulty versus those with low autism traits when perceiving an expression that would ordinarily appear negatively valenced following adaptation ($t(90) = 2.01, p < .05$; $t(90) = 2.47, p < .05$; $t(90) = 2.47, p < .05$). However, no group differences were evident for after-effect perceptions involving positive emotions ($t(90) = -1.73, p > .05$; $t(90) = .62, p > .05$). There were no group differences in the pre-adaptation emotion recognition task (all p 's $> .05$).

Conclusions:

The results show that people with high autism traits have difficulties producing representations of negative emotional expressions, but not positive ones. These findings have implications for understanding basic emotion processing in the broader autism spectrum.

141.087 87 Visual Fixation Patterns During Emotional Face-Voice Matching. R. B. Grossman*¹ and T. Mitchell², (1)*Emerson College*, (2)*University of Massachusetts Medical School Shriver Center*

Background: Individuals with autism spectrum disorders (ASD) have significant social communication deficits, particularly in the realm of non-verbal communication, such as maintaining eye contact, or the decoding of emotion from facial expressions and tone of voice, or prosody (Grossman et al. 2009, Shriberg et al. 2001). Eye-tracking data has also shown preferential gaze patterns to the mouth region of the face, rather than the eyes (Pelphrey et al. 2007).

Objectives: The purpose of our study was to use eyetracking to analyze the spatial and temporal looking patterns of adolescents with ASD and their typically developing (TD) peers in an emotional face voice matching task. Our hypothesis was that adolescents with ASD would show significant differences in the timing of gaze patterns to faces compared to their TD peers, and preferentially gaze to the lower, rather than the upper face.

Methods: We used eight semantically neutral sentences recorded in happy, surprised, sad, and angry emotions with high and low emotional intensity (Grossman et al. 2009). The 64 prosodic stimuli were presented to 25 adolescents with ASD and 25 TD controls. Participant groups were matched on age (mean = 12), IQ, and receptive vocabulary. After each sentence, participants saw two static facial expressions side-by-side on a computer screen. Their task was to determine which of the two faces was more likely to have spoken the preceding sentence. One facial expression in each pair matched the emotion and intensity level of the sentence. The other also matched on intensity level, but represented either an emotion with opposite valence (e.g. angry sentence with happy and angry facial expressions) or the same valence (e.g. angry sentence with sad and angry facial expressions).

Results: We recorded the percent of looking time to Area of Interest (AOIs) for trials with accurate responses and calculated a 2 (group) x 6 (AOI: upper face, lower face, eyes, mouth, face, and non-face) repeated measures ANOVA. Results show no group differences for overall looking time to any AOI and both groups spent significantly more time looking at the eyes than the mouth. However, the participants with HFA shifted their gaze from the fixation point located between face images to the non-face area of the correct image significantly later ($p = .008$) and also accumulated significantly more fixations to the non-face ($p = .01$) than the TD group.

Conclusions: Our data indicate that adolescents with ASD allocate overall looking time similarly to their TD peers during a face-voice matching task. They do not avoid the eye region or preferentially gaze at the mouth area of the face. There are, however, significant timing differences between the gaze patterns of the two groups. Adolescents with HFA shift their gaze from a central fixation location to the non-face of the correct image significantly later than their TD peers and return their gaze to the non-face significantly more frequently. Future analyses of gaze patterns to social stimuli in ASD should focus on timing, in addition to purely spatial differences.

141.088 88 Your Goal Is Not Mine: Absence of Mimetic Desire in Autism Spectrum Disorder. B. Forgeot d'Arc^{*1}, M. Lebreton², I. Soulières³, L. Mottron¹ and M. Pessiglione⁴, (1)*Centre d'excellence en Troubles envahissants du développement de l'Université de Montréal (CETEDUM)*, (2)*institut du Cerveau et de la Moelle*, (3)*University of Quebec in Montreal*, (4)*Institut du Cerveau et de la Moelle*

Background: The spreading of desires within a group is a form of social contagion that manifests not only in culture and learning, but also in rivalry and mob behaviour. A basic neural mechanism for this phenomenon has recently been demonstrated (Lebreton et al. 2012): adult participants in the general population rated objects as more desirable once perceived as the goals of another agent's actions. This *mimetic desire effect* relies on the modulation of the brain valuation system - a ventral striatoprefrontal network- by the mirror neuron system.

Some behavioural features of autism spectrum disorders (ASD) suggest a lower sensitivity to social influence: persons with ASD tend to develop

interests unrelated to those of their peers (American Psychiatric Association, 1994; Kanner, 1943); they have been reported to be less prone to flattery (Chevallier et al, 2011) and hypocrisy (Izuma et al, 2011). On the other hand, social influence in people with ASD may be manifested through the sharing of stereotypes prevalent in their social group (Hamilton & Krendl, 2007; Hirschfeld et al, 2007) or the influence of an observer on motor performance (Izuma et al 2011). Brain basis of mimetic desire effect may be atypical in ASD: disrupted long range connectivity is increasingly believed to be associated with ASD. Although more controversial, an atypical functioning of the Mirror neuron system has also been reported in ASD (Dapretto et al 2006).

Objectives: We assessed whether the mimetic desire effect is reduced in persons with ASD compared to persons without ASD.

Methods: Young adults with ASD and controls without ASD matched for age, IQ and gender took part to the study (current n of 10 per group; data collection still undergoing). Participants in the ASD group met ADOS-G and ADI-R thresholds and DSM-IV criteria for an ASD. All participants had FSIQ>85. Participants with self-reported depression (Beck Depression Inventory score>20) were excluded. Participants attended to a series of videos displaying objects. The objects were either the goals of an action performed by an actor (goal condition) or not (non-goal condition). The participants then rated to what extent they wanted to use the object. We performed an ANOVA to test the interaction between condition (goal vs non-goal) and group (ASD vs non ASD) on desirability rating.

Results: Participants from both groups used the desirability scale similarly (e.g. there was no significant difference in mean ratings and similar variability in scores). Nevertheless, there was a significant group by condition interaction on desirability rating. Participants without ASD gave significantly higher desirability ratings in the goal than non-goal condition ($p<0.05$), whereas ASD participants gave similar ratings in the goal and non-goal conditions ($p=0.45$).

Conclusions: Contrary to what was observed in control participants, the desires of persons with ASD were not influenced by others' actions. We

believe that this finding reflects a basic difference in susceptibility to social influence between persons with and without ASD, possibly contributing to the atypical development of interests and learning in ASD. The developmental course and neural underpinning of such difference remains to be explored.

Medical Co-Morbid Conditions Program

142 Medical Co-Morbid Conditions

This session has posters related to medical co-morbidities in ASD.

142.089 89 Association Between Sensory Behavior and Pupillary Light Reflex in Children with Autism Spectrum Disorders. C. L. Daluwatte¹, J. H. Miles^{*2}, J. Sun³ and G. Yao³,
(1)University of Missouri, (2)Thompson Center at the University of Missouri, (3)University of Missouri Columbia

Background: Atypical pupillary light reflexes (PLR) have been observed in children with autism spectrum disorders (ASD), suggests potential autonomic nervous system (ANS) dysfunction in ASD. ANS is also involved in modulating sensory processing and sensory processing problems are widely reported in children with ASD. However, the potential correlations between physical measurements (e.g. PLR) and behavioral observations (e.g. sensory) have rarely been examined in literature.

Objectives: To study the association between sensory behavior and PLR parameters in children with ASD.

Methods: We examined PLR in 259 children including 152 with ASD (age 10.7 ± 3.4 years) and 107 with typical development (TD) (age 10.9 ± 2.9 years). The test was conducted in both light adapted (LA) and dark adapted (DA) conditions using a two channel binocular apparatus. To quantify PLR responses, five basic PLR parameters were extracted including resting pupil diameter, relative constriction amplitude, latency, constriction velocity and redilation velocity. The parent or guardian completed a 29-item questionnaire adapted from Dunn (1994) designed to evaluate sensory behavior. Linear correlations were first applied to analyze the association between PLR parameters and sensory total score. Linear regression was then used to investigate whether variations in PLR parameters can be explained by a combination of sensory behaviors. The partial least squares (PLS) regression was performed to select a subset of

sensory behaviors as predictor variables that can explain the maximum variance in PLR parameters.

Results: PLR constriction amplitude correlated with the sensory total score ($r \approx 0.3$, $p < 0.02$) in the ASD group but not in the typically developing group ($p > 0.05$). No correlation was found between sensory total score and other PLR parameters. PLR constriction amplitude obtained in the ASD group at the highest stimulus intensity in light adaptation was best predicted in our regression analysis using the sensory item "Avoids getting messy" ($b = 1.4$ $p=0.017$) and "Has difficulty paying attention" ($b = 1.8$ $p=0.005$). Post-hoc one-way ANOVA revealed significant effects from items "Avoids getting messy" ($F=4.93$ $p=0.028$) and "Has difficulty paying attention" ($F=7.05$ $p=0.0088$) on PLR constriction amplitude in the ASD group. Children with ASD who reported "rarely" or "never" on the aforementioned two items had greater PLR constriction amplitude than those who reported "always". In the PLS regression model, the above two items plus 7 others were selected and can explain 11.1% of the data variance in PLR constriction amplitude.

Conclusions: A weak but significant correlation existed between PLR constriction amplitude and sensory total score in the ASD group but not in typically developing children. Lower PLR constriction amplitude suggests lower parasympathetic modulation. This observation implied that the abnormal sensory behavior in children with ASD could be associated with lower parasympathetic modulation.

142.090 90 Autism Symptoms and Behavioural Disturbances in ~500 Children with Down Syndrome in England and Wales. G. Warner^{*1} and P. Howlin², (1)Institute of Psychiatry, (2)Institute of Psychiatry, King's College London

Background: Recent research (DiGuseppi et al., 2010; Moss et al., 2012) shows that a significant minority of children with Down syndrome (DS) also meet diagnostic criteria for an autism spectrum disorder (ASD). These children demonstrate a distinct behavioural profile and have been reported to show higher levels of stereotyped behaviour, repetitive language, overactivity and self-injury than children with typical DS (Moss et al., 2012).

Objectives: The present study explored rates of autism symptoms and associated behaviour

problems in children aged 6-15 years with DS in England and Wales.

Methods: Potential participants (N=1382) were recruited via the UK Down's Syndrome Association. The Social Communication Questionnaire (SCQ; Rutter et al., 2003) was used to screen for autistic symptoms and the Strengths and Difficulties Questionnaire (SDQ; Goodman, 1997) to explore behavioural difficulties. The survey also investigated developmental regression.

Results: Questionnaires were completed by 507 families (37% of the cohort; however 8 responses were excluded because age was not indicated or fell outside the inclusion boundaries). The proportion of children who met the cut-off score on the SCQ for ASD (total score ≥ 15) was 37.7% (95% confidence interval [CI]: 33.4% - 42.0%) and for autism (total score ≥ 22) 16.5% (95% CI: 13.2% - 19.8%). Children who met the cut-off for ASD were significantly more likely to be reported as having emotional symptoms ($Z=5.48$, $p<.001$, $r=0.29$), conduct problems ($Z=5.96$, $p<.001$, $r=0.31$) and hyperactivity ($Z=8.15$, $p<.001$, $r=0.42$) on the SDQ than children who scored well below cut-off (total score <10). Developmental regression, in both language and general skills, was also higher in the ASD group. However, odds ratio analysis of item specific responses using an autism reference group (Moss et al., In press) indicated that the profile of their autism symptoms on the SCQ was atypical compared to children with idiopathic ASD.

Conclusions: The pervasiveness of ASD in children with DS in England and Wales is substantially higher than in the general population. These children experience significantly greater behavioural problems than children with DS only. Early detection of autistic symptoms is essential for the provision of appropriate intervention. However, the atypical ASD profile may affect the recognition of the disorder and inhibit the implementation of autism specific interventions.

References:

DiGuseppi, C., Hepburn, S., Davis, J., Fidler, D., Hartway, S., et al. (2010) Screening for autism

spectrum disorders in children with Down syndrome, *Journal of Developmental & Behavioural Pediatrics*, 31, 181-191.

Goodman, R. (1997). The strengths and difficulties questionnaire: A research note. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, 38(5), 581-586.

Moss, J., Richards, C., Nelson, L. & Oliver, C. (2012) Prevalence of autism spectrum disorder symptomology and related behavioural characteristics in individuals with Down syndrome. *Autism*, 0(0) 1-15.

Moss, J., Oliver, C., Nelson, L., Richards, C., & Hall, S. (In press). Delineating the profile of Autism Spectrum Disorder characteristics in Cornelia de Lange and Fragile X Syndromes. *American Journal of Intellectual and Developmental Disabilities*.

Rutter, M., Bailey, A., Lord, C. & Berument, S. (2003) *The Social Communication Questionnaire*. Los Angeles, CA: Western Psychological Services.

142.091 91 Autism and Maple Syrup Urine Disease: A Case Report.
R. Colak, S. Yilmaz and S. Herguner*, *NE University, Meram Faculty of Medicine*

Background: Autism is characterized by impairments in social interaction and communication and by restricted, repetitive, and stereotyped patterns of behavior. It is commonly accepted that the pathophysiology of autism is multifactorial. In most of the patients it is not possible to identify any etiological explanation in spite of extensive medical investigations. However, in about 10% of cases an associated medical condition is found. Maple syrup urine disease (MSUD) is a rare autosomal recessive metabolic disorder caused by a deficiency of the branched - chain 2 ketoacid dehydrogenase activity which leads to accumulation of toxic levels of branched chain amino acids (leucine, valine and isoleucine) in tissues and body fluids. MSUD has been associated with central nervous system damage, developmental delay, and neurocognitive deficits.

Objectives: According to our knowledge there is no reported case with both autism and MSUD.

Methods: We describe occurrence of autism in a girl with MSUD.

Results: The case is a 62 - month - old girl of a consanguineous 27-year-old mother and 31-year-old father. She was referred to our clinic for her self-injurious behaviors, aggression and sleep problems. During her assessment she had poor eye contact and no joint attention. She did not show reciprocity during social interaction. She also had repetitive behaviors such as rocking her body and flapping her hands. Her motor development was delayed: she sat at 15 months and walked 24 months of age. She did not develop phrases and had only 10 single words.

She had grand mal epilepsy and was on oxcarbazepine treatment. She was diagnosed as MSUD when she was 15 months of age and was on special education for her intellectual disability. In her family history her aunt had mental retardation and her cousin (female) had a diagnosis of MSUD. According to her psychiatric evaluation she had a diagnosis of autism disorder and moderate mental retardation. Childhood Autism Rating Scale and Autism Behaviour Checklist (ABC) were used to rate the severity of her autistic symptoms. Her ABC score was 93 and in CARS she had 48 that means high severity of autism symptoms.

Conclusions: Although a chance occurrence of these two conditions can not be ruled out, it is possible that MSUD might have played a role in the emergence of AD in this reported case. Studies on rats showed that alpha-keto acids accumulating in maple syrup urine disease stimulate lipid peroxidation and reduce antioxidant defenses in cerebral cortex. Neuroinflammation processes have been also suggested in the etiology of autistic disorder.

Routine metabolic investigation is not recommended in cases with AD. However several metabolic disorders (e.g. phenylketonuria, histidinemia) was found to be associated with autistic symptoms with a rate higher than that found in the general population. Clinicians who diagnose and treat metabolic disorders which are accompanied with mental retardation should be aware of possible diagnosis of ASD.

Samples. R. Sacco*¹, S. Giovinazzo², P. Curatolo³ and A. M. Persico⁴, (1)IRCCS "Fondazione Santa Lucia", (2)Univ. of Rome, (3)Univ. of Rome 'Tor Vergata', (4)University Campus Bio-Medico

Background: Several studies have reported a high frequency of epilepsy and/or co-occurrence of EEG abnormalities in children with autism spectrum disorder, although the incidence rates vary between 5% to 46%. The data heterogeneity reported in literature is probably due to the different characteristics of the samples examined in each study which may include different clinical features and ages. Many factors such as mental retardation, brain impairments and rare genetic diseases associated with ASD, increase the risk of epilepsy in symptomatic or syndromic autism. However, seizures or EEG abnormalities detected in "idiopathic" ASD remains higher than in general population, suggesting that autism is associated with a higher risk of epilepsy and EEG abnormalities. To this date it is not clear if this comorbidity represents an epiphenomenon of the neural dysfunction in autism, or if there may be a causal relationship between the two.

Objectives: To reconsider the mentioned association between epilepsy and/or EEG abnormalities with clinical, biological, developmental and familial medical history. We examined data extracted from two different large and selected samples of ASD patients.

Methods: We analyzed two different samples of non syndromic ASD patients: an original sample encompassing 432 Italian patients and a replica sample including 714 Caucasian American patients recruited by the Autism Genetic Resource Exchange Consortium (AGRE). Comparable clinical, biological and developmental variables were correlated in both samples with "presence/absence of epilepsy" or "presence/absence of EEG abnormalities", and tested for association between each variable and biological endophenotypes (serotonin blood levels, head circumference and global peptiduria), by non parametric Kendall τ , Kruskal-Wallis ANOVA and Mann-Whitney U test.

Results: In the experimental sample and in the replica sample, ASD patients positive for EEG abnormalities display a significant association with a lower risk of familial history for

autoimmune/allergic diseases (Italian and AGRE sample: $\tau = -0.115$ and -0.252 , respectively; both $P < 0.05$), and those affected by epilepsy are characterized specifically by verbal language delay in the absence of a generalized neurodevelopmental delay (Italian and AGRE sample: $\tau = 0.100$ and 0.073 ; both $p < 0.05$). Interestingly, Italian patients with EEG abnormalities show significantly lower serotonin blood levels ($\tau = -0.183$; $P < 0.01$).

Conclusions:

Overall, epilepsy and EEG abnormalities remain a relatively isolated and independent features, not strongly associated with specific symptom patterns. Nonetheless, these results extend previous findings, by supporting a deleterious effect of EEG abnormalities on verbal language development, and by pointing toward a protective role against the development of epilepsy for a family history of autoimmune/allergic diseases and elevated serotonin blood levels. These results spur interest into the potential positive effects of antiepileptic drug treatment in facilitating language development among small non-verbal ASD children with EEG abnormalities, even in the absence of overt seizures.

142.093 93 Early Diagnostic Differences Between Children Diagnosed with Autism Spectrum Disorders (ASD) and Children with Comorbid ASD and Mitochondrial Disease. K. N. Sargent^{*1}, R. Morris¹, D. L. Robins¹ and J. Shoffner², (1)*Georgia State University*, (2)*Medical Neurogenetics*

Background: The frequency of mitochondrial defects in ASD are not known, but individuals with oxidative phosphorylation (OXPHOS) defects appear to be at greater risk for symptoms associated with ASD compared to individuals with typical mitochondrial functioning. Mitochondrial disease exacerbated by fever appears to contribute to regression observed in the early development of children with ASD (Shoffner et al., 2010). Little is known about the early diagnostic similarities between children on the autism spectrum with and without mitochondrial dysfunction.

Objectives: While the ultimate goal is to understand how OXPHOS defects relate to neurologic features of some children with ASD, there is an immediate need for qualitative descriptions regarding the similarities and

differences between these two patient groups. Preliminary observations from our lab suggest that children with comorbid ASD and OXPHOS mitochondrial disease exhibit less consistent social deficits. Specifically, clinically important distinctions may be observed in diagnostic tools such as the Autism Diagnostic Interview, Revised (ADI-R; Rutter, LeCouteur, & Lord, 2003).

Methods: Children with a diagnosis of ASD alone ($n = 19$; 2 female; $M_{age} = 9.60$, $SD_{age} = 1.79$) and with a comorbid diagnosis of ASD and mitochondrial disease ($n = 16$; 2 female; $M_{age} = 8.87$, $SD_{age} = 2.16$) between the ages of 5 and 11 were recruited for participation in two independent fMRI studies investigating emotion processing and working memory, respectively. The comorbid diagnostic participants are part of a current ongoing research project, whereas the participants with known ASD only were included from a project ending in 2010. Each child's primary caregiver completed the ADI-R with a reliably trained graduate student or licensed psychologist in person or over the phone. The ADI-R Diagnostic Algorithm and total domain scores were used for the current analyses.

Results: Independent samples t tests were used to compare total scores between ASD only vs. comorbid ASD and mitochondrial patients' ADI-R total scores. The two groups did not differ with respect to age, $t(33) = -1.10$, $p = .28$. Patients with ASD alone were reported by their caregiver to demonstrate more severe social deficits ($M_{ASD} = 19.63$; $M_{MITO} = 13.94$), $t(33) = 2.21$, $p = .034$, $\eta^2 = .13$, as evidenced by ADI-R total Social Deficits domain score. Significant differences were not observed for the Communication Deficits domain score, $t(33) = 1.53$, $p = .14$, $\eta^2 = .07$, or the Restricted/Repetitive Behavior domain score, $t(33) = 1.16$, $p = .25$, $\eta^2 = .04$.

Conclusions: According to caregiver report on the ADI-R, it appears that children diagnosed with comorbid ASD and mitochondrial disease presented, on average, with less severe social deficits during their early social development. These data corroborate preliminary observations of work in our lab with children who have comorbid ASD and OXPHOS mitochondrial disease and suggest that further research is warranted investigating the interaction of OXPHOS or mitochondrial defects and ASD symptomatology.

142.094 94 Factors Associated with Irritability in Children with Autism Spectrum Disorder Compared to Children with Other Developmental Disabilities. M. D. Valicenti-McDermott*, K. Lawson, K. Hottinger, R. M. Seijo, L. H. Shulman, M. Schechtman and S. Shinnar, *Albert Einstein College of Medicine*

Background: It has been reported that children with Autism Spectrum Disorders (ASD) are more irritable than children with other developmental disabilities (DD). There are conflicting reports about associations between irritability and specific factors such as gastrointestinal and sleeping problems. However, it is possible that irritability in children with ASD is more related to these factors than for children with other DDs.

Objectives: To compare reported irritability in ethnically diverse children with ASD vs. those with other DDs and to assess the relationship of irritability to feeding/gastrointestinal (GI) and sleep problems.

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: Aberrant Behavior Checklist (ABC), GI Questionnaire and Child's Sleep Habits Questionnaire. Irritability was defined as scores above the 85th %ile on the ABC. Statistical analysis included chi-square, t test, correlations and regression.

Results: Mean age 8 3 yr; 15% White, 44% Hispanic and 24% African/American. Irritability was reported in 53% of the ASD group and 20% of the DD group ($p < 0.001$). Children with ASD presented more co-morbid symptoms: GI (66% vs. 40%, $p = 0.04$) and sleep problems (78% vs. 33%, $p < 0.001$). In the ASD group irritability was related to food selectivity with textures (58% vs. 13%, $p = 0.002$) and GI symptoms (88% vs. 59%, $p = 0.04$), especially diarrhea (65% vs. 35%, $p = 0.04$); there was no association with sleep problems (81% vs. 74%, $p = 0.7$) or food allergies (12% vs. 17% $p = 0.6$). In the DD group, irritability was associated only with sleep problems (70% vs. 25%, $p = 0.02$); there was no association with feeding/GI symptoms or food allergies. There were no associations between demographic characteristics and reported irritability for either group. The association

between irritability and ASD persisted after adjusting for demographic characteristics (including maternal education), sleep and GI problems. (OR 5.3 95%, CI 1.8-15.5).

Conclusions: In this ethnically diverse sample, children with ASD were more frequently reported to be irritable than children with other DDs. Factors associated with irritability included GI and food selectivity in the ASD group and sleep problems in the DD group. Interestingly, the association between ASD and irritability was independent of GI or sleep problems.

142.095 95 Fragile X, Intermediate, and Premutation Alleles in the Autism Genetic Resource Exchange (AGRE). W. T. Brown*, A. Glicksman, X. H. Ding, N. Ersalesi, C. Dobkin and S. Nolin, *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. ~35% of the first 480 families were noted to have had some genetic testing prior to entering the registry. The individuals receive ADI-R and ADOS.

Objectives: We have screened the FMR1 locus in one proband from each of 1742 families.

Methods: Standard Molecular Methods were employed

Results: We found 8 families that had the fragile X mutation present. 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 $\sim 40 \pm 25$). Previous prevalence studies of fragile X in autistic samples range from 0 to 16%; with a mean of $\sim 4\%$; (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). 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% is 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.

Conclusions: 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 0.78%. Among the 206 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 0.98%. 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%. Thus, 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.**

142.096 96 Gene Expression Profiles of Inflamed Ileocolonic Biopsy Tissue in GI Symptomatic ASD Children Are Consistent with an Inflammatory Bowel Disease. S. J. Walker*, *Wake Forest Institute for Regenerative Medicine*

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. Although distinct histologic and immunohistochemical properties of this inflammatory infiltrate have been previously described in this ASD^{GI} group, molecular characterization of these lesions has not been reported. Currently, it is not clear whether children with ASD and GI symptoms, coupled with non-specific mucosal infiltrates, have

conventionally recognized forms of IBD, a novel IBD phenotype, or no disease at all.

Objectives: The purpose of this study was to compare gene expression profiles (differentially expressed transcripts - DETs) in both ileal and colonic tissues in GI symptomatic ASD children (ASD^{GI}) with histologic inflammatory infiltrates and a non-ASD control group (non-pathologic tissue). The hypothesis being tested is that DETs in ASD^{GI} distinguish this group from non-inflamed controls, and provide further evidence of an inflammatory bowel disease (IBD) in the former group.

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 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^{GI} and control groups for each of the two tissues. Lists of DETs in ASD^{GI} were then evaluated for gene ontology and biological pathway involvement using the Ingenuity Pathway Analysis (IPA) software suite.

Results: Pair-wise analyses between ileal mucosa from ASD^{GI} and non-inflamed control samples resulted in 2570 DETs. Seventy-three percent (1862) of DET's were down-regulated in the ASD group compared with the control group while the remainder were up-regulated (@ fold change ≥ 2 ; adjusted $p \leq 0.05$). Analyses of inflamed colonic mucosa from ASD^{GI} children and non-inflamed controls resulted in 2393 DETs, 69% (1657) down-regulated in ASD^{GI} mucosa compared with those in the control group, while the remainder were up-regulated (@ fold change ≥ 2 ; adjusted $p \leq 0.05$). Two of the most highly significant disease categories returned by IPA in these tissues were *gastrointestinal disease* ($p = 1 \times 10^{-9}$

[TI] and $p = 3 \times 10^{-13}$ [colon]) and *inflammatory response* ($p = 1.7 \times 10^{-11}$ [TI]).

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 colon have a distinct molecular signature that is consistent with the larger disease categories of gastrointestinal disease, and more specifically, overlaps with Crohn's disease, ulcerative colitis, and autoimmunity.

142.097 97 Mental and Physical Health in Youth and Adults with Autism Spectrum Disorders in Ontario Canada: Findings From a Community-Based Sample. K. P. Stoddart*¹, L. J. Burke², B. Muskat³, J. Manett², S. Duhaime², C. Accardi² and P. Burnham Riosa², (1)University of Toronto, (2)The Redpath Centre, (3)The Hospital for Sick Children

Background: There has not been a major community-based survey in Canada since the 1990s on the profiles and service needs of youth (16+) and adults with ASDs. Since then, there have been significant changes to the definitions of this cluster of disorders in the DSM, and as a result, in the community a greater recognition of the entire range of ASDs. A contemporary understanding of the profiles of these individuals is essential in guiding the development of policy, research and service agendas.

Objectives: The objective of this study was to gather data on the clinical profiles and service needs of a large community-based sample of individuals 16 years of age and over with ASDs in Ontario Canada. Data was collected in the following areas: (i) Medical and mental health information; (ii) Life skills information; (iii) Service/support use, needs and costs; (iv) Social activities; and (v) Daily activities. In this report, summary data will be presented on medical and mental health information only.

Methods: Data was collected across the province of Ontario using an Internet-based questionnaire. The questionnaire was devised based on previous large-scale surveys on adults and in consultation with stakeholder groups. The study was advertised by school boards, agencies and organizations providing services and supports to youth and adults with ASDs. Upon an expression of interest in the study, respondents were required to verify that they were: (i) an individual diagnosed by a professional with an ASD or, (ii) a

family member of an individual diagnosed with an ASD or, (iii) a professional with knowledge of an individual diagnosed with an ASD. Participants completed one survey per individual identified with ASD; therefore, these findings represent the profiles of 490 unique youth and adults. The data was collected between August 2011 and August 2012.

Results: The sample was comprised of 72% males. The mean age of the sample was 29 years (SD=12). The findings indicate that many youth and adults with ASDs continue to receive their first diagnosis in adolescence and adulthood, although there is a significant difference in the age of diagnosis between the autism group and the Asperger Syndrome group. 42% of the sample had been accurately diagnosed with anxiety, 27% with depression, and a third felt that they were suffering from an undiagnosed psychological disorder. Overall, we found that there were high rates of health problems and extensive use of medications and complimentary treatments. Access to clinicians and health care providers who understand these needs are however limited, according to respondents.

Conclusions: Given that a recent epidemiological study of adults with ASDs in the UK suggested that 1% of the adult population there may have an ASD, it is critical that health policies and services parallel our emerging understanding of this cohort's physical and mental health needs and profiles gained through the collection of data from large community-based samples.

142.098 98 Mitochondrial Reserve Capacity in Peripheral Blood Mononuclear Cells Is Related to Development and Glutathione Redox Status in Children with Autism Spectrum Disorder. R. E. Frye*¹, S. Rose², J. Slattery³, R. A. Wynne³, S. Melnyk² and S. J. James², (1)Arkansas Children's Hospital Research Institute, (2)University of Arkansas for Medical Sciences, (3)Arkansas Children's Hospital

Background: Mitochondrial dysfunction is one of the most prevalent metabolic abnormalities affecting children with autism spectrum disorder (ASD), yet the prevalence and significance of mitochondrial dysfunction in ASD remains poorly understood.

Objectives: To determine the significance of mitochondrial function on cognitive development in children with ASD.

Methods: The cognitive development of fifteen children with ASD diagnosed with the autism diagnostic observation schedule (ADOS) was evaluated with the Vineland adaptive behavior scale (VABS). VABS scores ranged from 50 to 79. Fresh peripheral blood mononuclear cells (PBMCs) were obtained from whole blood collected in the fasting state. Mitochondrial function was measured in the PBMCs using the Seahorse 96 XF Analyzer (Seahorse Bioscience, Inc, North Billerica, MA) to measure real-time oxygen consumption rate during the sequential addition of pharmacological inhibitors. These measurements were performed at baseline and after the addition of 3 concentrations of 2,3-Dimethoxy-1,4-naphthoquinone (DMNQ), an agent that generates both superoxide and hydrogen peroxide. Parameters of basal respiratory rate, maximal respiratory rate and reserve capacity were derived from these mitochondrial measurements. For each parameter, the baseline value and the slope of the change in value with increasing DMNQ concentrations were analyzed in relation to the VABS scores. In addition, serum glutathione measurements were obtained on all participants and correlated with mitochondrial respiratory parameters.

Results: The baseline and change in **Maximal Respiratory Capacity** and **Reserve Capacity** were related to VABS scores. A *higher baseline Maximal Respiratory Capacity* [$F(1,8)=16.90, p<0.005$] and a *greater decrease in Maximal Respiratory Capacity* with increasing DMNQ doses [$F(1,8)=8.03, p=0.02$] was associated with a lower VABS score. Similarly, a *higher baseline Reserve Capacity* [$F(1,8)=13.25, p<0.01$] and a *greater decrease in Reserve Capacity* with increasing DMNQ doses [$F(1,8)=6.34, p<0.05$] was associated with a lower VABS score. Higher oxidized glutathione was related to a greater decrease in **Maximal Respiratory Capacity** ($r=-.68, p<0.05$) and **Reserve Capacity** ($r=-0.70, p<0.05$) when challenged with DMNQ while a higher reduced-to-oxidized glutathione ratio was related to a lower baseline **Reserve Capacity** ($r=-0.66, p<0.05$).

Conclusions: These data support the notion of the existence of a subset of ASD children with mitochondrial dysfunction and support the notion that abnormalities in mitochondrial function have clinical significance. Specifically, ASD children

with lower cognitive function appear to have abnormalities in **Maximal Respiratory Capacity** and **Reserve Capacity** in PMBCs. These data are consistent with the notion that PMBCs with **Maximal Respiratory Capacity** and **Reserve Capacity** abnormalities are associated with a more oxidized microenvironment. These data confirm the significance of mitochondrial dysfunction in ASD and suggest that cognitive development of children with ASD may be linked to mitochondrial function.

142.099 99 Molecular Characterization of Gastrointestinal Microbiota in Children with Autism (both with and without gastrointestinal dysfunction) and Their Neurotypical Siblings. S. V. Gondalia*, Swinburne University of Technology

Background: In addition to core behavioral symptoms of autism, reports of gastrointestinal dysfunctions such as constipation, diarrhoea, and abdominal bloating are common. These observations have stimulated investigation of abnormalities of intestinal microbiota in autistic patients. Disruption of normal neurodevelopment by bacterial products, including lipopolysaccharides, toxins and metabolites, has been theorized to contribute to autistic pathology. We note that not all autistic individuals suffer from GI dysfunction; only a sub-population is affected. Although numerous intestinal microbial abnormalities have been identified in autism, conflicting results have often been reported. The purpose of this study was to identify whether a difference exists between the resident GI microbiota in children with autism (with and without GI dysfunction) and their neurotypical siblings.

Objectives: Generally, the GI microbiota is influenced by diet and environmental sources. Therefore, this study was designed to identify differences (and/or similarities) of the gut microbiota in children with autism (with and without GI dysfunction) and their neurotypical siblings who share a similar environment.

Methods: Faecal samples from children with autism (without GI dysfunction: $n = 23$; with GI dysfunction; $n = 28$), healthy sibling controls ($n = 53$) were studied by using the bacterial tag encoded FLX amplicon pyrosequencing (bTEFAP) procedure.

Results: Differences in bacterial composition between cases and controls were evaluated by UniFrac and analysis of similarity matrices. Overall, Firmicutes (70%), Bacteroidetes (20%) and Proteobacteria (4%) were the most dominant phyla in the total sample. Although autism samples differed from control across several species-specific variables, there were no clinically meaningful significant differences between the groups. Nevertheless, when the autism group was divided according to GI dysfunction, several significant microbial differences were apparent, although, these were not consistent across individuals and showed substantial variation.

Conclusions: The data do not support an association between autism and gastrointestinal microbiota generally; however, the data do indicate that there is a sub-population within autism that experience GI dysfunctions which may be associated with aberrant GI microbiota. This study has implications for treatment strategies in autism aimed at manipulation of the microbiota to reduce GI dysfunction. Further research is required to determine the optimal approach (e.g. anti/pro-biotic, dietary) and such approaches may necessarily need to be tailored to individual patients based on clinical microbial findings. Other explanations for the gastrointestinal dysfunction in this population should be considered including elevated anxiety and self-restricted diets.

142.100 100 Neurological Abnormalities Among 16p11.2 Deletion and Duplication Carriers. K. J. Steinman^{*1}, S. J. Spence², M. B. Ramocki³, M. Proud³, E. Marco⁴, S. K. Kessler⁵, S. M. Kanne³, A. Stevens⁶, A. V. Snow², R. Bernier⁶, R. P. Goin-Kochel³, E. Hanson² and E. Sherr⁷, (1)Seattle Children's Research Institute, (2)Children's Hospital Boston, (3)Baylor College of Medicine, (4)University of California San Francisco, (5)Children's Hospital of Philadelphia, (6)University of Washington, (7)UCSF

Background: Deletions and duplications of 16p11.2 (del and dup 16p) are recurrent genetic variations recently found to increase the risk of autism spectrum and other neurodevelopmental disorders. While some small studies have identified neurologic abnormalities in individuals with del and dup 16p, the nature and prevalence of neurologic exam abnormalities have not been well-established in large cohorts.

Objectives: To characterize the neurological findings seen in a large cohort of individuals with

deletions or duplications of 16p11.2 from the Simons Variation in Individuals Project.

Methods: We performed neurologic examinations (including assessment for spinal and neurocutaneous abnormalities) on deletion carriers (del; $n=69$) and duplication carriers (dup; $n=61$) to define the range of findings in these groups. We used one-sample t -tests to assess whether head circumference (z -score for age) in each group differed significantly from the general population. Fisher's exact tests were used to assess for differences in frequency of individual neurologic exam findings between age groups: children (<11 years old), adolescents (11–17 years old) and adults (≥ 18 years old). Data collection and analysis are ongoing and presentation of findings will also examine the association of neurologic exam findings with autism spectrum disorder symptoms and cognitive abilities.

Results: Mean (\pm SD) age in months was 120 ± 96 for del (48 children, 18 adolescents, 3 adults) and 224 ± 207 for dup (33 children, 4 adolescents, and 24 adults). Head circumference z -scores for age were large for del (1.3 ± 1.0 ; $p<0.0001$) and average for dup (-0.19 ± 1.17 ; $p=0.3$). Abnormalities of speech articulation (del 81%, dup 24%), deep tendon reflexes (61%, 49%), appendicular tone (58%, 47%), and casual gait (36%, 27%) were prominent among both groups. Both groups also exhibited spinal curvature abnormalities (40%, 24%), sacral dimples (30%, 24%), and numerous but varied neurocutaneous findings (50%, 51%). Less common findings included facial tone and strength abnormalities (del 16%, dup 7%), truncal hypotonia (13%, 12%), and dysrhythmia (8%, 9%). Abnormalities of heel walking were seen almost exclusively in del (del 11/60, dup 1/39). Frequencies of specific neurologic findings differed ($p\leq 0.05$) based on age group for speech articulation, appendicular tone, and spinal dimples in del and differed ($p\leq 0.05$) based on age group for neurocutaneous findings, spinal curvature, articulation, truncal and appendicular tone abnormalities, and hopping in dup.

Conclusions: Deletions and duplications of 16p11.2 are associated with a variety of neurological abnormalities, some of which may manifest differently depending on the age of

assessment. While some of these neurologic abnormalities are common in populations with neurodevelopmental disorders, others – such as articulation and spinal abnormalities – may be more specific to 16p11.2 copy-number variations. Identification of these neurological abnormalities serves an important role in understanding the protean clinical consequences of these recurrent variants and their role in autism spectrum and other common neurodevelopmental disorders.

142.101 101 Outcomes of Children with Cochlear Implant-Assisted Hearing and Autism Spectrum Disorder. M. P. Charlton*, *Royal Victorian Eye and Ear Hospital*

Background: Cochlear implant clinics now select paediatric candidates solely on audiology criteria, predominantly that hearing aids cannot provide adequate amplification for speech and language development. Previously candidates were excluded because of disability, and particularly of Autism diagnosis, in the belief that children would not benefit from cochlear implantation. Limited literature published has presented negative outcomes of implanted children with Autism. Our study is the largest and first to examine outcomes with regard to cognitive ability.

Objectives: To examine communication and educational outcomes of implanted children with severe-profound hearing loss and Autism Spectrum Disorder in the context of cognitive ability.

Methods: Progressive longitudinal follow-up of 31 children implanted in the Royal Victorian Eye and Ear Hospital programme 1999-2012. Children were diagnosed using DSM-IV criteria, generally by a psychologist specializing in hearing impairment and Autism diagnosis using the ADOS and ADI-R. Diagnosis was confirmed by paediatrician and speech pathologist. All children had MRI and CT brain scans, with aetiologies of hearing loss recorded. Tests of non-verbal cognitive ability and of expressive and receptive language were chosen according to ages and abilities, most commonly Wechsler or Griffiths Scales, and the Preschool Language Scale. Children were included in the study once communication follow-up ('hearing age') was three or more years post-implant.

Results: Twenty-five children had communication assessments three-plus years post-implant. Mean

age of diagnosis of hearing impairment was 9.9 months (SD 9.0), and Autism 49.5 months (SD 20.7). Fourteen children had Normal cognitive ability (IQ 70 plus), and 11 had cognitive Disability (IQ below 70). There were no significant differences (.05 level) between Normal and Disability groups in mean age of diagnosis of hearing impairment, aiding, or implantation, or in age at cognitive or language assessment. Mean ages in months were: aiding 11.7 (SD 8.9), cochlear implantation 32.9 (SD 25.9), cognitive assessment 53.9 (SD 26.4), and communication 'hearing age' assessment 57.9 (SD 23.5). All Normal and 4 Disability group children had normal MRIs. Aetiologies were known in 21 children, with an acquired base (CMV or prematurity) in one Normal and 5 Disability group children, and the remainder genetic or structural. Seven Normal and no Disability group children had normal range oral communication results (standard score 70 plus), with significant group differences (receptive $\chi^2 7.6$ 1df $p=.005$, expressive $\chi^2 4.9$ 1df $p=.02$). Nine Normal group children were oral only, 4 used speech and Auslan sign, and 1 sign. In the Disability group, no child was totally oral, and children used limited sign or PECS. All children attended preschool intervention for hearing impairment; two Normal and 9 Disability group children attended centres for other disabilities. At school-age, 11 of 12 Normal and 3 of 8 Disability group children attended mainstream school with support, while the remaining 6 school-age children attended schools for children with disability.

Conclusions: Implanted children with normal cognitive ability and Autism can acquire functional oral language as their sole communication mode. Most attend supported mainstream school. Their outcomes are superior to those who also have cognitive disability.

142.102 102 Overgrowth in Autism Spectrum Disorders: Possible Link with Susceptibility to Seizures or EEG Abnormalities. G. Valvo¹, S. Baldini¹, F. Brachini¹, F. Apicella², A. R. Ferrari¹, R. Guerrini³, M. Marchese¹, F. Moro¹, F. Muratori², F. M. Santorelli¹, R. Tancredi² and F. Sicca*¹, (1)*Stella Maris Scientific Institute*, (2)*University of Pisa – Stella Maris Scientific Institute*, (3)*Meyer Pediatric Hospital, University of Florence*

Background:

Seizures occur in approximately 30% of individuals with Autism spectrum disorders (ASD); electroencephalographic abnormalities in an even higher percentage (about 60%). Onset of seizures in ASD shows bimodal distribution, with one peak occurring before 5 years and a later onset after 10 years. This comorbidity has led to identify an Autism-Epilepsy Phenotype (AEP) suggesting common pathogenetic pathways. However, the relationship between autism and epilepsy remains strongly elusive, making it difficult to detect shared pathophysiological and genetic underpinnings, mainly due to complexity of phenotypes.

Objectives:

We examined the phenotypic characteristics of ASD children, with and without epilepsy or EEG abnormalities, to assess whether autism-epilepsy represents a distinct clinical condition within the autistic spectrum. By reducing phenotypic complexity we attempted to subgroup AEP individuals, and provide new insight on the meaning of this comorbidity.

Methods:

A sample of 171 individuals with idiopathic ASD was divided in three experimental groups: 1. ASD and seizures; 2. ASD and EEG abnormalities, without seizures; 3. ASD, without seizures and with normal EEG. ASD diagnoses were confirmed using the Autism Diagnostic Observation Schedule (ADOS). Cognitive and socio-behavioral symptoms, as well as electroclinical and anthropometric parameters, were investigated to identify differences among groups, and the features that increase seizures risk in ASD. Continuous and categorical variables were analyzed respectively through ANOVA and post-hoc multiple comparisons, and Chi-squared test. A correspondence analysis was used to decompose significant Chi-squared and reduce variables dimensions.

Results:

The percentage of children with seizures (30.4%), and EEG abnormalities without seizures (32.2%), agreed with literature data, confirming that the prevalence of epilepsy in ASD clearly exceeds that

of the general population (0.5 to 1%). No differences emerged among groups at ADOS scores, showing that epilepsy (or EEG anomalies) as comorbid condition does not affect the core behavioral, communicative and social features which define ASD. Severe intellectual disability was also associated with seizures ($p = 0.030$). The rate of high stature (18%), moreover, was higher than expected in the general population (3%), showing that overgrowth in ASD may not be limited to the brain, but be more global involving the whole body.

The most relevant result was the significant association between isolated high stature (without macrocephaly) and EEG abnormalities ($p = 0.013$). Only 2/13 children with isolated high stature displayed seizures, at 10.8 and 15.1 years, therefore in the late peak of onset. Therefore, isolated high stature seems to be a risk factor for EEG abnormalities (without seizures), or for late onset seizures in ASD. Isolated macrocephaly, however, was equally distributed among groups, whereas only when accompanied by high stature was associated with seizures, with onset in the early peak.

Conclusions:

These results contribute to distinguish phenotypes within ASD heterogeneity. Seizures in ASD might be correlated with growth pattern. High stature could therefore be a potential biomarker of susceptibility to EEG abnormalities or late onset seizures in ASD. The "high stature\EEG abnormalities" phenotype could perhaps represent a distinct pathophysiological and genetic subtype in the autism spectrum.

142.103 103 Overweight and Obesity: Prevalence and Correlates in a Large Clinical Sample. K. Guion¹, L. Voltolina¹, J. B. Rouillet¹, M. Wolf¹, R. D. Steiner¹, K. E. Zuckerman¹, L. Huang-Storrs¹ and E. Fombonne^{*2}, (1)*Oregon Health & Science University*, (2)*Oregon Health and Sciences University*

Background: Previous studies have shown that the rate of obesity in children with autism spectrum disorders is significantly higher than that in the typically developing population, though consistent with rates of obesity being higher in other populations with chronic developmental disabilities (Rimmer et al 2010; Chen et al., 2010). Specific predictors of overweight and obesity in ASD children should be identified in

order to promote healthier life and inform clinical management

Objectives: To identify predictors of overweight and obesity in a clinical sample of children with ASD.

Methods: Data collected at the Oregon Health and Sciences University (OHSU) site of the Autism Treatment Network (ATN) on 388 diagnosed subjects (83% male; mean age: 5.4 years; range: 2.0 -16.9 years) were available. Overweight (OWT) and obesity (OBY) were respectively defined as a BMI \geq 85th or \geq 95th centiles derived from CDC population norms. Data on parental concerns, autism severity, adaptive behavior, verbal level, medication use, socio-demographic background were available through the ATN database.

Results: The mean BMI was 17.4 (17.5, boys; 17.3, girls) and the median was 16.5. Prevalence was 33.8% for OWT and 16.5% for OBY. Both OWT and OBY were unrelated to sex ($p > .50$). OVW ranged from 21% to 40% and OBY from 9.1% to 22.5% by age group. Age was not significantly associated with either OVW ($p = .10$) or OBY ($p = .48$).

Bivariate analyses showed that parental education level, ethnicity, verbal level of the ASD child, autism severity and diagnostic subtype were unrelated to OVW (all NS). Standardized scores of the Vineland did not vary by OVW status. OVW was also unrelated with high t-scores on subscales (anxiety, somatic complaints, attention, aggression, oppositionality) and broader band t-scores (internalizing, externalizing and total) of the CBCL (all p : NS). Correlations between BMI and CBCL continuous scores were small and nonsignificant. Most parental concerns (sleep, language, self-injury, aggression, adhd-type behaviors, mood swings, anxiety, sensory issues, repetitive behaviors) and, surprisingly, concerns about eating problems, were also unrelated to OVW. However, parental concerns about socialization difficulties were associated with child OVW ($p = .02$). No association was found with use of any psychotropic medication ($p = .27$) as well as with specific classes of medications. In a subsample of 94 children (mean age: 8.9 years; 87.2% male) with Stanford-Binet data, a trend

emerged for a negative association between full scale IQ and BMI ($r = -.19$; $p = .06$).

Analyses were repeated for OBY children and broadly comparable results were obtained. One exception was that melatonin use was significantly higher in OBY children than in their counterparts (32.8% vs 19.4%; $p = .02$). Comparisons with population norms and data from other atypical groups will be performed.

Conclusions: OVW and OBY were highly prevalent in this ASD clinical sample. Attempts to identify predictors of OVW and OBY were unsuccessful. In particular, none of the specific characteristics of autism predicted OVW or OBY, suggesting that the same risk factors apply for OVW and OBY occurring in ASD children ASD and typical and other atypical populations.

142.104 104 Parent-Based Sleep Education for Children with Autism—Role of Socioeconomic Status. K. W. Adkins¹, A. M. Reynolds², S. Weiss³, A. Loh³, T. Katz², S. E. Goldman¹, N. Madduri¹, T. Clemons⁴ and B. A. Malow^{*1}, (1)*Vanderbilt University*, (2)*University of Colorado Denver*, (3)*Hospital for Sick Children, University of Toronto*, (4)*The Emmes Corporation*

Background: Training parents to improve sleep habits in their children with autism spectrum disorders (ASD) has shown promise on sleep and child/family functioning, although factors associated with efficacy have not been well characterized.

Objectives: To examine biological and familial factors associated with efficacy in a parent-based sleep education for children with ASD.

Methods: We carried out a multisite protocol at three sites within our Autism Treatment Network. Children ranged in age from 2-10 years, with their clinical diagnosis of ASD (by DSM-IV criteria) confirmed by the Autism Diagnostic Observation Schedule. All had sleep onset delay, defined by a sleep latency of 30 minutes or greater. Children were evaluated for medical co-occurring conditions that affect sleep, and children with these conditions were either excluded or treated prior to enrollment in the protocol. Parents were randomized to individualized (1 one-hour session with 2 follow-up calls) or group (2 two-hour sessions with 2 follow-up calls) to: (1) Learn

techniques related to appropriate timing of sleep and sleep hygiene (e.g., daytime habits, evening habits, sleep environment); (2) Develop and implement an individualized bedtime routine; and (3) Discuss strategies to interact with their child to minimize bedtime resistance and night wakings. Two weeks of actigraphy were completed before and one-month after parent education. Bivariate and multivariate models were reviewed to determine the predictors of improvement in sleep latency, our primary outcome variable. Socioeconomic status (SES) was measured by the Hollinghead Four Factor Index, which incorporates parental education and occupational status.

Results: Data from 80 children [64 boys, 16 girls; ages 5.7 ± 2.6 years (mean \pm standard deviation)] were analyzed. As format of education (group vs. individual) did not influence outcomes, results were analyzed for the entire dataset. Actigraphy showed an overall improvement in sleep latency from 58.2 ± 29.1 minutes to 39.6 ± 21.4 minutes (change in sleep latency of 18.6 ± 26.9 minutes; $p < 0.0001$). Child age, gender, IQ, and medications did not affect sleep latency. Sleep latency was associated with SES, with a lower SES associated with a larger reduction in sleep latency ($p = 0.03$). The mean SES in our sample was 44.4 ± 12.3 .

Conclusions: Lower SES was associated with a greater improvement in sleep latency in our parent-based sleep education program. The reasons for our findings warrant further study. One explanation for our findings is that families of higher SES may have previously received effective sleep training through educational materials and formal therapies and have had less to gain than those of lower SES. Further study of the role of SES in parent education programs for children with ASD appears warranted.

Acknowledgement: This research was conducted as part of the Autism Speaks Autism Treatment Network. Further support came from a cooperative agreement (UA3 MC 11054) from the U.S. Department of Health and Human Services, Health Resources and Services Administration, Maternal and Child Health Research Program, to the Massachusetts General Hospital. The views expressed in this publication do not necessarily reflect the views of Autism Speaks, Inc.

142.105 105 Potential Link Between Anxiety and Insomnia in Individuals with Autism Spectrum Disorders. M. C. Souders*¹, C. M. Puleo², A. Bennett³, L. N. Berry⁴, I. Giserman⁵, W. T. Eriksen⁶, R. T. Schultz³ and J. D. Herrington⁷, (1)University of Pennsylvania/The Children's Hospital of Philadelphia, (2)Temple University, (3)Children's Hospital of Philadelphia, (4)Texas Children's Hospital, (5)The Children's Hospital of Philadelphia, (6)University of Pennsylvania School of Nursing, (7)University of Pennsylvania

Background: One of the most common co-occurring medical conditions in individuals with ASD is chronic, severe insomnia, with a prevalence estimate of 60-80% (Wiggs & Stores, 2004; Souders et al., 2009). One hypothesis for elevated insomnia in ASD is hyper-arousal, which may be related to altered levels of excitatory neurotransmitters (Bourgeois, 2007). Hyper-arousal is also a key component of many anxiety disorders, and more than half of children with ASD experience clinically significant problems with anxiety (Sukhodolsky et al., 2008). Although it appears likely that hyper-arousal, anxiety and insomnia are related in ASD, we presently have only a limited understanding of this relationship.

Objectives: The purpose of this study was to investigate the nature of the relationship between anxiety symptoms, biomarkers of arousal dysregulation and sleep parameters in children and adolescents with ASD as compared to typically developing controls (TDC).

Methods: Sixty individuals with ASD, ages 6-17, were compared to 16 TDC. Participants had their ASD diagnosis confirmed by ADOS/ADI. Anxiety symptoms were evaluated via the Anxiety Disorders Interview Schedule (ADIS-C/P, a two-hour child and parent clinician administered interview), and multiple parent-administered anxiety questionnaires. Sleep was characterized by 5-7 nights of actigraphy (a micro-computer that measures movement), sleep diaries, sleep questionnaire and a comprehensive medical interview. Diurnal urine samples were obtained the evening and night prior to the center evaluation, in order to measure catecholamine levels (an index of arousal). The evaluation also included measures of heart rate, respiration, skin conductance and temperature with the Biopac MP150 and BioHarness.

Results: The current, first phase of the analysis included summary statistics and cross-tabulations, followed by a Fisher's Exact test. A DSM-IV-TR anxiety diagnosis was identified with the ADIS-C/P in 28/58 of the ASD subjects (48%). One of the 16 TDC participants was identified with a specific phobia. 53% of the ASD subjects had an insomnia diagnosis based on sleep diaries, actigraphy, questionnaires and history. Two of the 16 TDC had insomnia (12.5%). We found a significant association ($p < 0.0001$) between Anxiety Diagnosis and an Insomnia Diagnosis in individuals with ASD (25/28). Only 6 individuals with ASD without anxiety had insomnia (6/30). In the second phase of the analysis we will be correlating anxiety questionnaires and sleep measures. We will also be analyzing the urine samples for norepinephrine, epinephrine, cortisol and melatonin levels.

Conclusions: This preliminary analysis suggests that anxiety and insomnia are closely linked. We expect that after the completion of the analysis we will have greater insights into the relationship between arousal dysregulation, anxiety, and insomnia in ASD. This understanding will ultimately lead to more targeted co-treatment of anxiety and insomnia in ASD.

142.106 106 Prevalence of Overweight and Obesity in Youth with Autism Spectrum Disorders. R. P. Nash^{*1}, E. Park¹ and L. Sikich², (1)University of North Carolina at Chapel Hill, (2)ASPIRE Research Program, UNC-CH

Background: Overweight and obese children are at an increased risk for physical, social, and psychological disorders as compared to the general population. In addition, early weight gain predisposes children to adult obesity. Many developmental and psychiatric disorders have been associated with a higher prevalence of obesity and overweight, as compared to the general population. Research has suggested that children with Autism Spectrum Disorders (ASD) are at 2-3 times greater risk for obesity and overweight than typical peers. However, these results have been based on parent-reported height, weight, and diagnosis [1,2].

Objectives: Our aim was to determine the prevalence of objectively measured obesity and overweight in a large group of ASD youth and compare it with measured rates in the US population.

Methods: We utilized the National Database for Autism Research (NDAR), which includes reports of standardized ASD diagnostic measures (ADI and ADOS), demographics and physical exams gathered from multiple studies. We extracted height, weight, and demographic (gender, age, race/ethnicity) data for 249 children between the ages of 2 and 17 who met criteria for ASD by ADI and/or ADOS. We calculated age- and sex-specific BMI percentiles for each subject and determined the percentage of subjects whose BMI percentiles met criteria for underweight ($< 5^{\text{th}}$ percentile), overweight ($\geq 85^{\text{th}}$ percentile), and obesity ($\geq 95^{\text{th}}$ percentile). These data were compared to those from the general population, as collected by the National Health and Nutrition Examination Survey (NHANES) (2009-2010) and reported by Ogden, et al [3].

Results: In the general population, 31.8% of children are overweight and 16.9% of children are obese [NHANES database; Ogden et al, 2012]. In comparison, we found that 43.8% of children meeting criteria for ASD by ADI and/or ADOS were overweight, and 25.7% were obese. An increased prevalence of obesity and overweight amongst children with ASD was not specific to one particular demographic; the percent of overweight and obese children with ASD was elevated compared to the general population across the majority of ethnic, age, and gender groups considered.

Conclusions: Children with ASD have a much higher prevalence of obesity and overweight than the general population and are likely to experience more long-term health consequences. Excessive weight in ASD youth might be due to multiple factors including medication use, opportunities for prolonged physical activity and engagement in age appropriate activities. We are particularly concerned about treatment with second generation antipsychotics, which are the only agents with an FDA indication in ASD, but are also associated with heightened weight gain and insulin resistance. Further analyses incorporating additional data available from NDAR will examine the correlation of overweight/obesity with medication history, cognitive abilities and level of social functioning in order to help elucidate the particular aspects of ASD that predispose this population to increased weight. The areas that

appear most strongly associated should be targets of intervention development efforts.

1. Curtin et al (2010) BMC Pediatrics, 10(1),11-5.
2. Rimmer et al (2010) J Intellectual Disability Research, 54(9), 787–794.
3. Ogden et al (2012) JAMA, 307(5), 483–490.

142.107 107 Relationship Between Salivary Cortisol and Serum Testosterone in Boys with Autism. A. M. Neumeyer^{*}1, A. Gates², C. Ferrone² and M. Misra¹, (1)Massachusetts General Hospital/ Harvard Medical School, (2)Massachusetts General Hospital

Background: Data are limited regarding the hormonal profile of children with autism spectrum disorders. Adrenal hormones such as cortisol are increased in conditions of stress and in turn mediate the physiological response to stress. Some studies have reported that children with ASD have a lower diurnal variation of cortisol compared with controls. Data are conflicting regarding levels of gonadal hormones such as testosterone in ASD, with some (but not all) studies reporting higher testosterone levels in this condition. Data are also conflicting regarding levels of thyroid hormones in ASD.

Objectives: Our objective was to examine levels of cortisol, testosterone, TSH and free thyroxine in peripubertal boys with ASD versus controls, and particularly to determine the diurnal variation in salivary cortisol and its relationship with serum testosterone and free T4 levels.

Methods: In 18 peripubertal boys (mean age 10.5±0.4 years) with ASD and 19 age matched controls (11.2±0.3 years) (p=0.23) 8-14 years old, we measured morning levels of testosterone, IGF-1 and free T4, and 8 AM and 11 PM salivary cortisol .

Results: The morning levels of serum testosterone, IGF-1, free T4 and TSH, and 8 AM salivary cortisol did not differ in children with ASD compared with controls. However, the 11 PM salivary cortisol was higher (1.44±0.37 vs. 0.47±0.16 nmol/L, p=0.004), and the ratio of AM/PM salivary cortisol lower in boys with ASD compared with controls [reported as median (25th

quartile- 75th quartile) using a non-parametric test (Wilcoxon rank sum test); ASD: 1.14 (0.60-3.81); Controls: 3.36 (1.96-6.33), p=0.03]. In controls, testosterone levels correlated positively with IGF-1 (rho=0.59, p=0.008) and 11 PM cortisol (rho=0.60, p=0.01), and inversely with free T4 (rho= -0.48, p=0.04). In boys with ASD, associations of testosterone with IGF-1 (rho=0.68, p=0.003) and with free T4 levels (rho= -0.60, p=0.01) were preserved, however, the association of testosterone with 11 PM cortisol was lost (rho=0.14, p=0.60). There were no associations of testosterone, IGF-1 or free T4 with the AM/PM cortisol ratio in either group.

Conclusions: This is the first study to describe a loss in the relationship of PM salivary cortisol with AM serum testosterone in peripubertal boys with ASD compared to controls. . Associations of testosterone levels with other hormones such as IGF-1 and free T4 are preserved in boys with ASD. Further studies are necessary to better understand the implications of these findings.

142.108 108 Motor Abnormalities in Children with Phelan-McDermid Syndrome and Autism Spectrum Disorders. K. Bellesheim*, T. Tavassoli, A. Kolevzon, L. Schwartz and J. D. Buxbaum, Mount Sinai School of Medicine

Background:

One of the more common monogenic causes of autism spectrum disorders (ASD) is a deletion or mutation of the *SHANK3* gene on chromosome 22. Deficiency of the *SHANK3* gene, also called Phelan-McDermid Syndrome (PMS), accounts for 0.5-1 percent of cases of ASD. Children with PMS show autistic symptoms including speech abnormalities, developmental delay, and motor deficits. Many children with PMS undergo oral-motor therapy to improve difficulties in chewing, swallowing, and sucking, issues that can lead to life-threatening complications in this population. Motor abnormalities are clinically reported in PMS and ASD; however, research that analyzes motor deficits associated with PMS or ASD is limited.

Objectives:

In order to better understand the development of motor abnormalities such as poor muscle tone in children with PMS and the broader autism spectrum, the present study sought to compare

the muscular activation of one of the main muscles responsible for chewing, the masseter muscles. We aim to compare 15 children with PMS, to 15 children with ASD, to 15 typically-developing children. Specifically, the current investigation aimed to quantify empirically-based differences in the process of mastication in PMS as described by clinically-reported hypotonia and, if these differences exist, to see whether or not the results extend to the broader ASD population.

Methods:

Participants included children ages 6-12 years who had a primary diagnosis of PMS, ASD, or typically-developing children. Muscular activation of the muscles used for chewing, the masseter muscles, was measured using electromyography (EMG), an instrument that detects the electrical activity produced by skeletal muscles. Each of the three groups underwent a surface EMG. Three electrodes were attached bilaterally above the right and left masseter muscles. The data was encoded using a ProComp Infiniti system. During the procedure, participants chose a solid food item, e.g. bite-sized pieces of potato chips. Each child completed an initial baseline and five trials of chewing followed by a recovery baseline period. Using Biograph Infiniti software, minimum, maximum, and mean baseline and chewing scores were calculated.

Results:

Preliminary results demonstrate that children with PMS have lower mean masseter muscle baselines, lower maximum peaks, and overall lower mean electrical activation of their masseter muscles compared not only to the typically-developing children, but also to the broader ASD group. Furthermore, children with ASD have lower muscle activation compared to typically-developing children.

Conclusions:

The present study is the first scientific investigation to specifically explore motor abnormalities in PMS. We found that children with PMS and/or ASD show hypotonia, having lower muscle activation as compared to typically-developing children. Future research should

increase the number of muscle groups and motor activities measured. The current findings of lower muscle activity in PMS and ASD have clinical implications; for example, muscular activation could be used as a biomarker in treatment studies.

142.109 109 The Child Sleep Habits Questionnaire in Children with Autism Spectrum Disorders. T. Katz*¹, S. E. E. Goldman², B. A. Malow², A. Shui³, S. J. Asghar², A. Bennett⁴, K. Byars⁵, H. Connolly⁶, D. Glaze⁷, S. E. Levy⁴, M. T. Ott⁴, I. Perez⁸, A. M. Reynolds¹, K. Sohl⁹, M. C. Souders¹⁰, S. Weiss¹¹ and M. Witmans¹², (1)University of Colorado Denver, (2)Vanderbilt University, (3)Massachusetts General Hospital for Children, (4)Children's Hospital of Philadelphia, (5)Cincinnati Children's Hospital Medical Center, (6)University of Rochester Medical Center, (7)Baylor College of Medicine, (8)Children's Hospital Los Angeles, University of Southern California, (9)University of Missouri - Thompson Center, (10)University of Pennsylvania School of Nursing/The Children's Hospital of Philadelphia, (11)Hospital for Sick Children, University of Toronto, (12)University of Alberta and Stollery Children's Hospital

Background: The Child Sleep Habits Questionnaire (CSHQ) asks caregivers to describe their children's sleep behaviors. The CSHQ has been validated for typically developing children ages 4-10 (Owens, Spirito, McGuinn, 2000), but there is little research examining its psychometric properties in children with autism spectrum disorders (ASD).

Objectives: To examine the factor structure, sensitivity, and specificity of the CSHQ in children with ASD from ages 2 to 17.

Methods: We analyzed data from children enrolled in the Autism Treatment Network (ATN) Registry. Parents of children ages 2 to 17 who had clinical diagnoses of ASD (based on DSM-IV criteria) confirmed by the Autism Diagnostic Observation Schedule and a DSM-IV interview completed the CSHQ. The sample was divided into three age groupings: 954 children ages 2-3, 2036 children ages 4-10, and 397 children ages 11 to 17. Cut-off values for sensitivity and specificity of the CSHQ were determined using published normative data (Owens, et al) and ROC analyses of the ATN data. The factor structure of the CSHQ was examined in each of the three age groups specified.

Results: After first identifying poor sleepers by parent report of sleep concerns on an intake questionnaire, ROC analysis of the CSHQ indicated that cut-off scores for optimal sensitivity and specificity fell within the range of 47-50 (ages 2-3), 46-55 (ages 4-10), and 44-46 (ages 11 to 17). We used a cut-off score of 47 for all three groups. Specificity was higher in all three groups when compared with the published cut-off score of 41 (51.48 vs. 81.03 for ages 2-3; 50.57 vs. 79.16 for ages 4-10, and 62.31 vs. 86.15 for ages 11 to 17.) Increasing the cut-off score decreased sensitivity (89.87 vs. 74.05 for ages 2-3; 90.94 vs. 66.96 for ages 4-10, and 83.21 vs. 67.18 for ages 11 to 17.) We examined a 2 and 3 factor solution of the CSHQ. Bedtime Resistance and Sleep Anxiety had the highest loadings for both the 2 and 3 factor solution for all three groups.

Night Wakings also loaded onto the first factor in the 2 factor solution for children ages 11+. Depending on the age grouping and number of factors, Parasomnias, Sleep-Disordered Breathing, Sleep Onset Delay, Night Wakings, Sleep Duration, and Daytime Sleepiness loaded onto either the second or third factor for the 2 or 3 factor solutions.

Conclusions: Based on our findings, a cut-off score of 47 greatly increases the specificity of the CSHQ. Factor analyses indicate that insomnia questions as well as questions related to other sleep difficulties (such as sleep disordered breathing and Parasomnias) are important for all age groups.

This research was conducted as part of the Autism Speaks Autism Treatment Network. Further support came from a cooperative agreement (UA3 MC 11054) from the U.S. Department of Health and Human Services, Health Resources and Services Administration, Maternal and Child Health Research Program, to the Massachusetts General Hospital. The views expressed in this publication do not necessarily reflect the views of Autism Speaks, Inc.

142.110 110 The Relationship Between Sleep and Health-Related Quality of Life Amongst Children with Autism Spectrum Disorders. J. Delahaye¹, D. Sikora², T. Hall³, F. Orlich⁴, E. Kovacs⁵, T. Clemons⁶ and K. Kuhlthau^{*7}, (1)Massachusetts General Hospital, (2)Providence Neurodevelopmental Center for Children, (3)Oregon Health and Science University,

(4)University of Washington, (5)Columbia University, (6)The Emmes Corporation, (7)Harvard Medical School

Background: Evidence shows that children with Autism Spectrum Disorders (ASD) experience significantly more physical and psychological health problems than typically developing peers. While these co-morbidities make ASD particularly difficult to diagnose and treat, they also create considerable health-related quality of life issues (HRQoL) for children and their families. Sleep problems are amongst the most prevalent of these co-morbidities, with an estimated 40- 80% of children with ASDs experiencing some type of sleep-related disturbance.

Objectives: This study examined the relationship between health-related quality of life and sleep problems in a large cohort of children with ASD. Aspects of HRQoL explored included physical and school functioning and emotional and social well-being. Sleep domains assessed included sleep duration, night waking, parasomnias, sleep disordered breathing, daytime sleepiness, bedtime resistance, sleep anxiety, and sleep-onset delay.

Methods: We recruited 100 parents of children with ASD through the Autism Treatment Network (ATN) and 2 large academic medical centers. HRQoL and sleep characteristics were assessed via parent-proxy, using the generic (non-condition specific) version of the Pediatric Quality of Life Inventory (PedsQL 4.0) and the Child Sleep Habits Questionnaire (CSHQ). Key clinical characteristics, such as behavior problems and ASD diagnosis and severity, were also analyzed. We examined descriptive data and used linear regressions with HRQoL summary variables as the outcome and sleep problem summary and sub-scale scores as the key independent variables. We ran regressions with the sleep problem scores alone and controlling for covariates (socio-demographic characteristics, behavioral problem scores, and autism severity scores).

Results: Regression analyses showed a consistent relationship between health-related quality of life and sleep problems, with several significant associations found amongst PedsQL and CSHQ scores. HRQoL total and summary scores were significantly associated with the CSHQ total score, with worse sleep problems indicative of poorer quality of life. Significant associations were also

found amongst PedsQL scores and CSHQ subscale scores in the expected direction, with a particularly strong relationship between sleep duration and HRQoL.

Conclusions: The associations found amongst sleep and HRQoL variables indicate that children's quality of life is adversely impacted by the experience of sleep problems, especially those related to sleep duration. Additionally, these results suggest that treatments that are effective in treating sleep disturbances may improve children's quality of life.

142.112 112 Verbal Ability As a Predictor of Sleep and Gastrointestinal Comorbidities in Children with Autism Spectrum Disorder. R. S. Mankoo¹, K. Hughes², T. N. Takahashi³, B. J. Ferguson⁴ and K. Sohl^{*1}, (1)*University of Missouri*, (2)*University of Missouri Thompson Center for Autism and Neurodevelopmental Disorders*, (3)*University of Missouri Thompson Center for Autism & Neurodevelopmental Disorders*, (4)*University of Missouri-Columbia*

Background: Autism Spectrum Disorder (ASD) is a complex neurodevelopmental disorder with known medical comorbidities. Associations between ASD, gastrointestinal dysfunction, sleep difficulties, and verbal communication ability have been suggested in previous studies. It is hypothesized that the ability of ASD patients to communicate verbally influences the ability of parents and physicians to recognize the presence of comorbid conditions.

Objectives: This study seeks to identify the prevalence of gastrointestinal dysfunction and concurrent sleep difficulties in ASD patients, and subsequently determine if the ability to communicate verbally alters the prevalence of these comorbidities.

Methods: The Thompson Center for Autism and Neurodevelopmental Disorders' patient database provided a study population of 338 eligible patients (Autism= 197; Aspergers= 34; PDD-NOS= 107). Parent-reported questionnaires from individual ASD patients were assessed for: gastrointestinal dysfunction (constipation, loose stools, other generalized GI complaint), sleep dysfunction (trouble falling asleep, trouble sleeping in one's own bed, achieving inadequate hours of sleep, nighttime awakening), and verbal communication status (ADOS module 1= nonverbal, ADOS modules 2-4= verbal). Data

was analyzed using Microsoft Excel and SPSS statistics software.

Results: Of the 338 study patients, 138 (40.8%) reported gastrointestinal dysfunction, and 139 (41.1%) reported problems with sleep. This study identified an increased prevalence of sleep dysfunction in patients with concomitant gastrointestinal difficulties (42.0%) compared to patients without reported gastrointestinal problems (40.5%). There was an increased prevalence of gastrointestinal dysfunction in patients with adequate verbal communication skills (73.2%) compared to patients who were classified as non-verbal (26.8%). In addition, there was an increased prevalence of sleep dysfunction in verbal patients (62.6%) versus non-verbal patients (37.4%).

Conclusions: This study concludes that the prevalence of sleep difficulties in ASD patients is enhanced by concurrent gastrointestinal dysfunction, while verbal communication status serves as a positive predictor of these ASD comorbidities. These findings suggest that the diagnosis of gastrointestinal or sleep dysfunction may be overlooked in many nonverbal ASD patients, indicating the need for modification of screening procedures for ASD comorbidities currently used in clinic. Future analyses of larger patient populations such as that provided by the Autism Treatment Network database, or physician-completed patient data forms rather than parent-reported questionnaires would serve as a strong comparative tool to the findings of this study.

Treatment Trials: Behavioral Interventions Program

143 Treatments: Interventions Focusing On Family (parent training, parent variables, siblings, etc)

This session focuses on trials involving the families and caregivers of children with ASD.

143.113 113 Parent Mediated Early Intervention in Young Children with Autism Spectrum Disorder (ASD): A Systematic Review and Meta-Analysis. I. P. Oono^{*1}, E. Honey¹ and H. McConachie², (1)*Newcastle University*, (2)*Institute of Health and Society, Newcastle University*

Background: Young children with ASD lack understanding of how to interact with another person, may not have developed language or understand other people's communication, and may insist on routines and repetitive behaviours.

This early pattern of difficulties is a challenge for parents. Therefore, helping parents to develop strategies for interaction and management of behaviour is an obvious route for early intervention. Though there is considerable support for early intervention for children with ASD, there is a need for systematic review of the quality of the evidence.

Objectives: To determine the level of current evidence for effectiveness of parent-mediated early intervention in the treatment of young children with ASD, assessing outcomes for both children with ASD and their parents. This is an update to an earlier Cochrane Collaboration review which found only 2 randomised controlled trials (RCTs) (Diggle, McConachie & Randle 2002)

Methods: We carried out in-depth literature searches in relevant databases including Ovid Medline, PsycINFO and CINAHL, for articles published between 2002 and August 2012. Relevant articles describing RCTs were then systematically evaluated for risk of bias and synthesised for child and parent outcomes using the Cochrane Collaboration guidelines for systematic reviews. In the meta-analysis, we combined numerical data (endpoint means and standard deviations) only across studies with a similar theoretical basis that used outcome measures of similar psychometric and psychological properties. Data were analysed using Review Manager Software version 5.1

Results: We identified 17 studies published from six countries (USA, UK, Australia, Canada, Thailand and China), recruiting a total of 919 child participants. Ten studies which evaluated intervention focusing on parent interaction style in facilitating children's communication were combined in meta-analyses. The evidence for positive change in parent-child interactions is strong (Shared attention time: SMD 0.41, CI = 0.14 to 0.68, $P < 0.05$ and Parent synchrony: SMD 0.90, CI = 0.56 to 1.23, $P < 0.05$). The evidence also tends to suggest effectiveness of parent-mediated approaches in improving child language outcome (direct assessment: SMD 0.45, CI = -0.05 to 0.95, $P > 0.05$) and child reported communication skills (MD 5.31, CI = -6.77 to 17.39, $P > 0.05$); and reduction in autism severity (SMD -0.31, CI = -0.65 to 0.03, $P = 0.07$) and parent stress (SMD -0.17, CI = -0.70 to 0.36, $P >$

0.05). However, the strength of the evidence is judged 'uncertain', failed to reach statistical significance and likely to change with future publication of high quality RCTs.

Conclusions: Though we now have 17 RCTs for review as opposed to 2 ten years ago, the evidence of the effectiveness of parent mediated interventions is still inconclusive and requires further research

143.114 114 A New Model of Therapy Mediated by Parents for Children with Autism and Pervasive Developmental Disorder. C. Napolitano¹, G. Valeri^{*2} and S. Vicari³, (1)Paediatric Hospital Bambino Gesù in Rome, (2)Children's Hospital Bambino Gesù, (3)Paediatric Hospital Bambino Gesù

Background: The social impairment, communicative, attentive and play skills shared reduce opportunities for children with Autism and Pervasive Developmental Disorder (PDD) to take advantage of natural experiences of everyday interaction. The development of socio-communicative skills in PDD was, in fact, the key objective of years of research from which they originated many types of therapeutic intervention. Our contribution concerns a model of Therapy Mediated by Parents (TMG) experienced at the outset, at the UOC Neuropsychiatry Bambino Gesù Children's Hospital in Rome. This model aims to enhance mutual communication and social interaction in a setting starring children and their parents. These become mediators of the proposed therapy in the clinical setting, proposing it to the child in his daily environment.

Objectives: The aim of this pilot study is to test the efficacy of a Therapy model Mediated by Parents in increasing the communication skills of children with PDD, compared to usual rehabilitation treatments.

Methods: A randomized controlled trial involving 26 children (20 boys and 6 girls; M age = 4.55 years; SD = ± 1.03) who met criteria for PDD and their parents participated in the study. All children followed a psychoeducational therapy by less than 1 year. For the sperimental group was added the TMG.

Both groups were administered the following tests at T0 and T1.

- **ADOS** (Lord et al 2000)

- **ADI-R** (Lord et al 1994)
- **GDMS - ER** (Griffith,2006)
- **Vineland** (Sparrow, Balboni, Pedrabissi, 2001)
- **PVB** Primo Vocabolario del Bambino (Caselli, Casadio, 1995)
- **PSI** Parent Stress Index (Abidin, 1995)
- **CBCL** Child Behavior Checklist (Achenbach, 2001)

To encode the intervention and make it repeatable, we created a detailed manual of TMG . To this end, meetings have been provided training for therapists before treatment and after the feedback meetings and interim post TMG treatment in order to standardize the structure of the manual.

The treatment consists of 6 monthly meetings as follows:

1. Psychoeducation and focus attention on the interest of the child
2. Posture to encourage interaction
3. Using simple language and appropriate
4. Reinforcement of communication
5. Promotion of the child's
6. Route calculation and verification key points

Each session lasts 50 minutes di TMG in the first part

is devoted to role playing exercises focused on the theme of the meeting and the last part is delivered to the parents a memorandum with the key points of the session and a homework to be done at home under discussion at the next.

Results: The comparison between the two groups after treatment showed a significant difference in the scale of communication dell'ADOS for the group that followed the TMG.

Conclusions:

A first analysis of data shows a statistically significant difference between the experimental group and control groups in the area of communication, both measured A) on a scale with dell'ADOS and B) on the percentage of children who become verbal (defined as: use of more than 5 words). Overall, the other parameters analyzed did not differ significantly the two

groups. In order to further verify the effectiveness of the treatment we propose to increase the sample, systematically measure and carry out follow up at 6 months and a year

143.115 115 Brief Parent Training for Parents of Children with Autism Spectrum Disorders: An Exploration of Parents' Stage of Change and Implications for Treatment. S. Wilson-Loupée*, *The Chicago School of Professional Psychology*

Background: Parent training has emerged as a robust intervention to help remediate developmental, adaptive, and behavioral challenges characteristic of children with Autism Spectrum Disorders (ASDs). However, parents' adherence to prescribed treatment regimens is generally suboptimal and not well understood. Although researchers consistently acknowledge parent adherence as an important determinant of child outcomes, few studies exist that address this issue. As it applies to ASDs, the first study to explicitly examine parents' adherence found that only 54% of parents sampled reported adherence to their recommended behavioral regimen. A distinct but related literature - pediatric chronic illness - observes equally disappointing findings. Similar to parents of children with ASD, parents of children with chronic illness are increasingly required to perform interventions at home. Across literatures, scholars have argued for an overarching model from which to conceptualize and address parent non-adherence to parent training initiatives.

Objectives: The purpose of this study was to (1) present the first use of the URICA in an ASD parent training sample, and (2) examine the relationship between motivation to change and several variables often cited in parent training literature as barriers to adherence. Based on findings in pediatric chronic illness literature, we predicted that motivation to change would be significantly correlated with information-seeking and behavioral knowledge. Likewise, we predicted that parents' sense of competency and family life impairment would vary in predictable ways depending on parents' stage of change classification. Since this is an exploratory study and the first to use the URICA, we also examined the association between motivation to change and satisfaction with parent training services.

Methods: Stage of change, information-seeking behavior, behavioral knowledge, parent sense of

competency, and family life impairment were examined before and after parents' participation in a brief parent training program. Parents' satisfaction with programming was also assessed after completion of parent training. Parents were enrolled in the parent training program as a gateway to accessing a broad range of clinical services. All program objectives were taught with the expectation that participating families will receive ongoing services at the clinic and that their individual therapist will continue to build on the skill set acquired through the program.

Results: Data collection is in progress.

Conclusions: Parents' adherence to parent training is a critical and understudied aspect of treatment for ASD. Findings from this study will add to this literature.

143.116 116 Comparison Between Special Education and “Keshet”- Parental Training Integrative Program- Can the Parents Choose?. L. Gabis*¹, M. Lux², T. Pilowsky Peleg³, S. Shefer⁴, R. Sofrin⁵ and J. Evron⁵, (1)*Tel Aviv University*, (2)*Safra Children's Hospital*, (3)*Tel Aviv Yaffo Academic College*, (4)*The sheba medical center The Weinberg child development center*, (5)*Sheba Medical Center, Weinberg Child Development Center, Israel*

Background:

Improvement in cognitive and communicative ability of children with autistic spectrum disorder (ASD) was associated with improved quality of life of children and their parents. Previous studies have found that this improvement is possible through intensive treatment of multidisciplinary team which starts at a young age. However, it remains unclear what therapeutic framework provides a comparable improvement to special education setting.

Objectives:

The current study was planned to evaluate and compare the effectiveness of two different frameworks of treatment for young children with autism spectrum disorder (ASD) and overall developmental changes during one year of intervention:

1. Special Education kindergarten framework, for children with communication deficits

which enables adjustments to the unique needs of children with ASD all week long.

2. Keshet- an inclusion program that enables participation of parents during individualized treatments of their children, including parental guidance in a triadic/diaadic model, for one day and a half (ten hours). During rest of the week, children are attending a regular kindergarten, thus involving extensive exposure to the normative peers group during the week- designated as Advanced Health program (AH).

Methods:

Twenty nine children with ASD, between the ages of two to six years old, participated in one of two treatment programs. All children in both groups received intensive multidisciplinary treatments, with at least ten hours of individualized treatment per week and tailored according to their developmental level, resembling DENVER-STAART model, while the Keshet group received all treatments in the presence of their parents, and the SE group in individual setting with additional weekly parental guidance.

Children's IQ and ADOS-G scores were compared at the beginning of the intervention program and after completion of one year of participation.

Results:

Pre-intervention - children in both groups did not differ in their autism severity, cognitive abilities and age, at the date. After one year, both groups showed significant improvements in Full Scale IQ (FSIQ), verbal (VIQ) and ADOS-G imagination/creativity (AI) scores. The quantified improvement was not significantly different between the two intervention programs. However, separate analyses within each group, showed different trends of improvement; thus children in the SE framework improved significantly only in their AI scores, whereas children in the AH framework improved significantly only in their FSIQ scores.

Conclusions:

Choice of inclusion versus special intervention program at preschool age, was not guided by severity level. All children with ASD, regardless of treatment program, improved over one year of intensive intervention, mainly in their cognitive abilities, but not in overall autism severity as measured by ADOS. Intervention in an inclusive program demands parental training and effort, but bears the possibility of equal improvements to special education setting.

143.117 117 From the Community to the Lab (and back): Identifying Important Treatment Components of a Parent Training Intervention. B. Ingersoll*, *Michigan State University*

Background: Project IMPACT is a parent training program for young children with ASD based on best practices that teaches social communication within daily routines and interactions (Ingersoll & Dvortcsak, 2010). This program was developed within community settings with the express purpose of identifying program elements that would assist community providers in implementing parent training.

Objectives: To better understand *how* the intervention affects parent and child behavior, we conducted a series of controlled evaluations in a lab setting using single-subject design (SSD) methodology.

Methods: Two, multiple-baseline SSDs were conducted with young children with ASD to evaluate the active ingredients of the intervention. In study 1, therapists implemented the intervention with young children with ASD (n=9) for 2-hrs per week for 8 weeks to examine the efficacy of the intervention package. In study 2, parents were trained to use the intervention with their children with ASD (n=8) once or twice per week for 12 weeks to evaluate the efficacy of the parent training model. Child language use was examined using behavioral coding of session tapes.

Results: The children increased their rates of expressive language during treatment in Study 1, providing preliminary evidence for the efficacy of the intervention package when implemented by trained therapists. The parents increased their use of the intervention techniques in Study 2, providing preliminary evidence for the efficacy of the parent training model. Improvements in the children's expressive language were also

observed, although results were not as robust with parents as with therapists. A panel analysis with fixed effects for concurrent time series designs demonstrated a significant association between parents' use of individual intervention strategies and their child's language use. Specifically, parents' use of responsiveness-based strategies (following the child's lead and imitating the child) and language prompting were both unique predictors of children's spontaneous language use within session.

Conclusions: The results provide preliminary support for the efficacy of key components of a parent training program that can be feasibly implemented in community preschool settings, and identify the active ingredients of the intervention (responsiveness-based strategies, language prompting). The next step is to empirically evaluate the effectiveness of the intervention in preschool programs, as implemented by community providers.

143.118 118 Linear Versus Multiphase Models Testing Outcomes for Infants At-Risk for ASD in a Randomized Controlled Trial of a Parent-Mediated Intervention. G. T. Baranek*¹, L. R. Watson¹, L. Turner-Brown², S. Field³, E. Crais¹, L. Wakeford¹ and L. M. Little⁴, (1)*University of North Carolina at Chapel Hill*, (2)*University of North Carolina at Chapel Hill*, (3)*Frank Porter Graham Child Development Institute, University of North Carolina at Chapel Hill*, (4)*University of North Carolina at Chapel Hill*

Background: Studies of early behavioral interventions for toddlers with ASD are emerging (Carter et al., 2011; Dawson et al., 2010), but little research examines the efficacy of interventions with infants **at-risk** for a later diagnosis of ASD in community samples. Intervening with infants at-risk prior to full emergence of diagnostic symptoms may be more efficacious and has implications for prevention.

Objectives: (1) Evaluate preliminary efficacy of a parent-mediated intervention (Adapted Responsive Teaching [ART]) for one-year-olds at-risk for ASD in improving child developmental outcomes and parent responsiveness. (2) Compare the ability of linear versus multiphase growth models to summarize within-subject variation in outcome variables across two study phases (short-term: pre- to post-treatment; long-term: post-treatment to follow-up).

Methods: This RCT tested effects of ART versus a control condition (Community Services [CS]), using an intent-to-treat analysis. Infants identified through birth records were screened for ASD risk with the First Year Inventory at 12 months of age; scores >95th% were assessed and subsequently enrolled. Using a 2:1 randomization ratio, 16 families enrolled (ART=11; CS=5). ART families received a 6-month home-based intervention designed to enhance parent responsiveness and child social-communication and sensory-regulatory functions. We compared linear and multiphase models as models for growth across the two phases of interest. Initial estimates for the unknown parameters from both models were obtained using maximum likelihood estimation (MLE). Small sample sizes motivated us to adopt a Bayesian simulation approach (Yuan & MacKinnon, 2009). We simulated sampling from the posterior distributions of model parameters using the Monte Carlo Markov Chain (MCMC) method implemented by the software WinBugs (Lunn, Best & Spiegelhalter, 2000).

Results: Despite the small sample, interval estimates from MCMC and MLE were largely similar; thus we report the more commonly used MLE method. The more parsimonious linear model provided a better fit for only a few variables, 3 of which demonstrated statistically significant associations between treatment assignment and post treatment growth (i.e., ART improved CSBS-CQ total score & Mullen Receptive Language, and worsened on SEQ Hyperresponsiveness). With multi-phase models, statistically significant associations between treatment status and growth were concentrated in the first (active treatment) phase of the study. After the first phase, 5 outcomes had significant treatment impacts – specifically, ART parents were less directive (MBRS) and their children showed less sensory hyporesponsiveness (SEQ) and higher levels of expressive and receptive communication and socialization (Vineland). In contrast, statistically significant differential growth by treatment status in the second, follow-up phase was largely absent. AIC statistics indicated that the multi-phase model provided a better fit than the linear model for all 5 of these variables.

Conclusions: Although some variables showed linear trends, the multi-phase model was preferred in most cases. Findings supported

greater gains for ART versus CS, although these gains were concentrated in the first (pre- to post-treatment) phase, while growth in the second phase (post-tx to follow-up) was substantially attenuated. Gains in socialization, communication, and sensory functions, as well as in parent behaviors, provide preliminary support for this parent-mediated intervention. Issues of maintenance of treatment effects require further research.

143.119 119 Evaluating Interventions in Autism: A Parent Educational Group Program. K. L. Berquist^{*1}, G. Y. Lee², C. M. Ardel² and A. Y. Hardan³, (1)Stanford University School of Medicine/Lucile Packard Children's Hospital, (2)Stanford University, (3)Stanford University School of Medicine

Evaluating Interventions in Autism: A Parent Education Group Program

Kari Berquist, Grace Lee, Christina Mich & Antonio Hardan

Background: Despite the availability of more than 966 interventions, there is no clear standard treatment for children with autism. In fact, the majority of these treatments have no or limited empirical support. Currently, decisions about intervention adoption is left up to parents, which are typically not scientific-based and are usually the result of the recommendations of professionals, friends, family, and/or the internet. A previous case series of a manualized individual treatment package found that parents can learn how to evaluate the effectiveness of the interventions their child's receiving. In light of these promising findings, replication studies are warranted using more efficient treatment delivery approach such as a group model.

Objectives: The purpose of this study is to examine the effectiveness of a 12-week parent education group program in targeting parent's evaluation skills (e.g., choosing an appropriate research design, operationally define target behaviors, taking reliable data) and scientific-based decisions (e.g., using objective ways to determine if treatments are effective). We hypothesize that parents participating in the study will exhibit improvement in their abilities to evaluate interventions their child's receiving and increased reliance on scientific-based evidence.

Methods: Parents of children with autism spectrum disorder between the ages of 3 to 13-years were invited to participate in this study. Diagnosis was based on an expert clinical opinion and confirmed with Autism Diagnostic Observation Schedule. Three group series were conducted over a 24 month-period. Each 12-week parent education program included weekly group or individual sessions (eight 90-minute group sessions and four 60-minute individual sessions). Primary measures included a standardized assessment to examine evaluative behaviors conducted at baseline, week 6, and week 12 and rated by a blind investigator. In addition, a semi-structured parent interview regarding parents' decision-making was completed at baseline and week 12 and rated by a blind investigator.

Results: This study is ongoing, and to date 22 participants have completed the parent education group program. Preliminary findings replicated previous findings on this manualized program. Parents who participated in the parent education group program significantly improved in their evaluation skills from pre- to post-intervention ($Z = 4.015$ $p < 0.000$) and their likelihood of determining effectiveness using scientific means ($Z = 3.051$ $p < 0.002$). In addition, ancillary data collected suggest that parents started, stopped, avoided, or modified the use of 24 different interventions as a result of using tools learned during the study.

Conclusions: Preliminary findings suggest that, compared to baseline levels, parents participating in a parent education group program resulted in significant changes in parent's evaluative skills, and scientific-based decisions. Findings from these preliminary studies suggest that parents of children with autism can learn how to evaluate the effectiveness of the treatment their children are receiving, and warrant future controlled studies to examine the value of this group model in a larger sample.

143.120 How Does Parent Inclusion in Playground Teaching and Parent-Child Interactive Style Affect the Effectiveness of EIBI On Play and Peer Engagement of Children with ASD?. K. Strauss^{*1}, M. Esposito², G. Valeri³, S. Vicari³, B. Monopoli⁴, M. T. Dipierro⁵ and L. Fava², (1)Autism Treatment and Research Centre "Una Breccia nel Muro", (2)Autism Treatment and Research Center "Una Breccia nel Muro", (3)Child Neuropsychiatry Unit, "Children's Hospital

Bambino Gesù", (4)Autism research and treatment center, (5)autism treatment and research center "Una Breccia nel Muro"

Background:

A variety of naturalistic interventions aim to account for increasing adult's responsiveness to the child and the quality of social engagement with the therapist and parent. In previous research (IMFAR 2012: 131.075) we found that adult-mediated intervention without direct naturalistic behavior intervention in the school setting facilitates the child's quality of play behaviors. Nevertheless, the child's pro-social responsivity on social interaction bits of others and child initiated engagement was achieved only with limitation to the guidance of an adult. As a consequence a previous EIBI program (Fava & Strauss, 2011) was adapted, including quasi-natural environments (small class-room & play groups) into clinical settings, combining parent and teacher treatment provision (Fava et al., 2012).

Objectives:

The aim of the current study was (1) to evaluate the effects of an EIBI program on play behaviors and joint engagement with and without parent inclusion in the playground teaching; (2) to understand the parent-child interaction characteristics that best facilitate social learning opportunities.

Methods:

30 children with ASDs were enrolled in a comprehensive EIBI program, with 16 children (14M:2F; $M_{age} = 45.7$ months, $SD = 10.22$) receiving naturalistic playground teaching without parent inclusion, whereas 14 children (10M:4F; $M_{age} = 38.8$ months, $SD = 9.98$) followed the parent inclusion condition. At baseline, and each 4 weeks (4 total measurement-points) children's social play and peer engagement was observed during free play for a total period of 12 weeks. The Play Observation Scale (Rubin, 2001) has been utilized to obtain information on child play behaviors, the Playground Observation of Peer Engagement (POPE; Kasari, 2005) on the child's joint engagement stages, a system by Anderson et al. (2004) on the quality of social interactions and

the Maternal Behavior Rating Scale-R (Mahoney et al. 1999) on parent-child interaction styles. Data collection and analysis currently needs to be terminated. Preliminary results indicate that children following the parent inclusion condition show an accelerated growth in play behaviors and engagement stages. These indications are the basis for detailed analysis.

Results:

Study aim (1) will be addressed applying General Linear Models comparing progress in play and peer engagement between both treatment conditions. We do expect to verify the preliminary result of an accelerated child development in the parent inclusion condition across all measurement points. Further, after adjusting for child characteristics we will control progress for confounding variables such as e.g. quality of supervision, group size etc. As effectiveness of parent inclusion in playground teaching over solely staff teaching seems supported, study aim (2) will examine the influence of parent-child interaction styles. Applying regression analysis, it is expected that parental responsiveness generally predicts increased social engagement, while a more directive style facilitates cognitive growth in object play. Additional moderator-mediator models aim to specify the role of parent affective behaviors that may differentially affect the linkage between parental interaction style and child behaviors.

Conclusions:

By identifying parent-child interaction styles that influence teaching strategies and promote the child's play and joint engagement, the results of this study can suggest models for parental teaching that can be incorporated into early childhood interventions.

143.121 121 The Effects of Parental Intervention On Emotion Recognition of Children with ASD: Preliminary Results of a Randomized Controlled Trial. R. Rosenan*, T. Gev, H. Avital and O. Golan, *Bar-Ilan University*

Background: Emotion and mental state recognition difficulties form a core deficit of individuals with ASD. Previous attempts to teach emotion recognition to children with ASD have yielded limited results, especially on

generalization to everyday life. Parental intervention was used in many therapeutic protocols for children with ASD and has been found successful in improving children's behavior, language, and social skills. Little is known about improvement of emotional development, including emotion recognition.

Objectives: To evaluate the effect of parent intervention on children's ability to learn emotion recognition from an animation series focusing on emotions and social situations. Emotion Tutoring Parent Intervention (ETPI) included a systematic and structured parent-child program provided to parents in a guidebook. The program consisted of conversation, play, and reading activities related to a selection of 16 basic and complex emotions and mental states. It provided an opportunity to teach children about emotions in a natural and experiential way, in order to boost generalization. The parent-child activities were based on the different emotions and mental states presented in the animation series.

Methods: Participants in this preliminary report of an ongoing study were twelve children with high functioning ASD, aged 4-7 years. Each child received a DVD of an animation series, and watched it for 10 minutes per day for 8 weeks. Parents of half of the children were also provided with the ETPI guidebook, and were asked to implement it on a daily basis, for at least 20 minutes per day. Measures were taken before and at the end of the intervention period. Measurements included computerized emotion recognition tasks and a verbal emotion definition task.

Results: After 8 weeks of intervention, children whose parents used the ETPI achieved higher scores on a computerized emotion recognition generalization task than the children whose parents did not use the ETPI.

Conclusions: The Emotion Tutoring Parent Intervention may promote emotion recognition skills and their generalization, among children with ASD. This preliminary data demonstrates how the impact of existing interventions, or even recreational activities (such as watching a TV series) could be boosted through the use of structured and systematic parent-child activities. It also demonstrates how parent might imbed

naturalistic and mutually enjoyable activities focusing on emotion tutoring into the child's daily life, in order to promote emotional development.

143.122 122 An Approach to Assessing Parent-Child Interaction in Autism. F. Larkin^{*1}, S. Guerin¹ and J. A. Hobson²,
(1)University College, Dublin, (2)Institute of Child Health, UCL

Background: Relatedness-focused interventions seek to remediate the core features of autism through improving interactions with others, often engaging parents as facilitators of their children's development (Dawson et al., 2010; Green et al., 2010; Gutstein, 2009; Kasari et al., 2010; Mahoney & Perales, 2003; 2005; Rogers et al., 2006; Wieder & Greenspan, 2003). The emergence of these interventions requires the development of outcome measures that demonstrate reliable and valid assessments of parent-child interaction (Lord et al., 2005).

Objectives: We examined the validity and reliability of two coding schemes for parent-child relatedness in school-age children with autism, and conducted a preliminary study on the feasibility of these measures for assessing treatment outcome in future studies.

Methods: Participants were 40 children between the ages of six and 14, and their parents. Twenty of the children (16 boys, 4 girls) were diagnosed with autism, and twenty of the children (16 boys, 4 girls) formed a heterogeneous comparison group. The groups were matched for IQ (Autism $M = 91.6$; Comparison $M = 88.9$). Dyads participated in a thirty-minute semi-structured assessment of parent-child interaction involving opportunities for joint attention, experience sharing, co-creation and collaboration (RDA; Gutstein & Sheely, 2002). The RDA was subsequently coded by separate sets of blind judges for time spent in states of Joint Engagement (Adamson et al., 2009) and states of a) Interactive Regulation and b) Intersubjective Engagement. Inter-rater reliability was excellent (ICC range .75 - .82).

Comparisons were made to standardised measures of autism severity (Autism Diagnostic Observation Schedule, ADOS: Lord, Rutter, DiLavore & Risi, 2001 and the Social Responsiveness Scale, SRS: Constantino & Gruber, 2005), the Parent Child Relationship

Inventory (PCRI: Gerard, 1994), and a more global coding of quality of parent-child interaction (Dyadic Coding Scales, DCS: Humber & Moss, 2005) which has been applied successfully to school-age children with autism (Beurkens, Hobson, & Hobson 2012).

Five of the children with autism receiving a relationship-based intervention were prospectively matched with five children with autism not receiving the intervention, and the measures were repeated one year later (with blind coding of baseline and outcome data), in order to provide preliminary information on the feasibility of this approach for assessing change over time during treatment.

Results: Dyads containing a child with autism spent more time in the following states:

-- Joint Engagement: 'Supported Engagement', suggesting caregivers were working harder to sustain joint focus.

-- Interactive Regulation: 'Contingency without Elaboration', an interaction-pattern characterised by rigidity and lack of flexibility/variation.

-- Intersubjective Engagement: 'Coordination of Actions', where partners engage by telling each other what to do, and attempt to control each other's actions, rather than engage with each other's intentions or feelings.

For the ten children with autism and their parents, taking part in the preliminary feasibility study, outcome coding is in progress and will be reported.

Conclusions: Coding schemes for parent-child interaction will allow better evaluation of intervention studies, and will offer clinicians tools to plan and evaluate relationship-based interventions.

143.123 123 The Impact of Parent Training On Parents' Use of Specific Pivotal Response Treatment Strategies. C. Pacia^{*1}, H. E. Flanagan², I. M. Smith³, K. Meko² and D. Chitty²,
(1)University College Cork, (2)IWK Health Centre, (3)Dalhousie/IWK Health Centre

Background: Pivotal Response Treatment (PRT) has been shown to be effective at promoting

communication in children with autistic spectrum disorders (ASD; National Standards Report, 2009). Parent training is an integral component of most PRT programs (e.g. Koegel & Koegel, 2006), and brief parent training in PRT strategies can lead to important gains (e.g., Coolican et al., 2010). More research is needed about the impact of different training models on parents' use of specific PRT strategies.

Objectives: To evaluate the impact of a parent training model that provides individualized, in vivo coaching in the use of PRT principles for 2 hours per day over 4 consecutive days. We examined (1) how often parents were using specific PRT strategies prior to training; (2) whether training led to significant increases in parents' use of specific PRT strategies.

Methods: Parents of 10 preschool children participated in the study (mean age 50.85 months; 9 males and 1 female). We obtained 10-minute videotaped probes of parents encouraging their children to communicate pre- and post-training. Coders used 1-minute interval recording to rate parents' use of 6 specific PRT strategies. Inter-rater reliability was fair to moderate for all but one strategy (following children's lead; excluded from analyses).

Results: Prior to training, parents often provided language opportunities when children were attending (60% of intervals), and sometimes provided clear language opportunities (49% of intervals). However, they rarely contingently reinforced appropriate communication, provided natural reinforcers, or reinforced good attempts at communication (all <25% of intervals). Paired-sample t-tests were used to compare pre- and post- training scores for each PRT strategy. Following training, there were significant gains in parents' skills providing clear language opportunities (increased to 80% of opportunities), contingently reinforcing appropriate communication (increased to 51% of intervals), providing natural reinforcement (increased to 51% of intervals), and reinforcing good attempts at appropriate communication (increased to 50% of intervals; all $p < .01$). There was no change in parent's skills providing language opportunities when children were attending ($p = .27$).

Conclusions: The present findings suggest that this model of parent training is effective at teaching parents most PRT strategies. Parents had the most difficulty with aspects of PRT related to the provision of contingent, natural reinforcers both prior to and following training. Ongoing training may be needed to maintain and extend gains. The level of parent skill in PRT that is required to improve children's language learning remains to be determined.

143.124 124 Parents and Their Toddlers with Autism: The Impact of the More Than Words Parent-Training Program. V. Smith*¹ and S. Patterson², (1)University of Alberta, (2)University of California, Los Angeles

Background:

According to best practice guidelines, including and training parents to assist their child's communication development is considered essential for effective autism intervention and a natural step to provide consistent, daily support for development (National Research Council (NRC), 2001). Research suggests that parents can learn to be effective language facilitators (Kaiser & Hancock, 2003); however, less is known about what constitutes effective delivery of parent training programs and further, even less is known about how effective these programs are outside the constraints of controlled research settings. Many parent-training programs are implemented without careful examination of whether and how well parents are able to learn skills taught and whether and to what extent their ability to use these skills alters the language environment.

Objectives:

This study utilized multiple methods of data collection to explore growth and change in parent-child interactions, parent skill development, and child language development in the child's natural language learning environment at multiple time points before, during and after parents' participation in the widely used parent language education program *Hanen More Than Words (MTW; Sussman, 1999)*.

Methods:

Fourteen male and 4 female toddlers who ranged in age from 24-39m (mean=30m) with a

developmental age of 2-28m (mean=12m) and their parents participated in the study. Thirty three percent of the families spoke a language other than English and 58.3% were Caucasian. All children had a diagnosis of autism or suspected autism.

Measures: Four methods of data collection were used in this study. First, the MacArthur Communicative Development Inventory (Words and Gestures Module) (Fenson et al., 2007) was utilized to track prelinguistic gestures, receptive and expressive language development. Second, in home parent-child talk audio (including adult word count, child vocalizations and conversational turns) was collected via a the Language Environment Analysis (LENA) system, a digital language processor. Third, child engagement in dyadic interaction was explored using videotape data and coded using a protocol developed by Bakeman and Adamson (1984). Last, parents and clinicians provided evaluations of the parents' skills via a 24-item questionnaire.

Results:

Overall, these families spoke at rates lower than average demonstrated by families of typically developing toddlers (Gilkerson & Richards, 2008). Parents increased their skill mastery from 10% at baseline to approximately 50% post intervention. Children demonstrated statistically significant changes (paired sample t-tests) in their receptive language ($t(10)=-2.75$, $p=0.020$, $d=.662$), prelinguistic gestures ($t(10)=-2.12$, $p=0.060$, $d=.440$), and their frequency of coordinated joint attention in dyadic interaction ($t(8)=-2.67$, $p=0.028$, $d=.957$).

Conclusions:

Results indicate that parents' response to the program was not uniform. Four patterns of change in the timing, quality and quantity of parent-child talk and child language were observed. Where, in families where both adult talk and child language increased, children demonstrated greater increases in coordinated joint attention, receptive and expressive language while parents demonstrated higher fidelity. The opposite was true in families where little to no change occurred in adult talk or child language. Discussion will

include consideration of the importance of child and parent characteristics when examining the impact of parent training.

143.125 125 Promoting Social Responsiveness Between Primary Caregivers and Children with Autism. E. (. M. Maher*,
University of Sydney

Background:

Difficulties in the development of the capacity and desire to reference others, communicate to share subjective experiences and establish joint attention are core characteristics of autism. Evident in very young children with autism, these deficits have profound effects on the development of cognition, communication and social relating.

Objectives:

This study involved implementation of a caregiver training program conducted over a 6-month period, derived from a developmental social pragmatic orientation, and using the Relationship Development Intervention (RDI) Program model (Gutstein, 2009). The goal was to determine whether an increase in adult-initiated declarative bids was more successful at facilitating experience-sharing and child responsiveness than bids that were imperative in nature.

The study examined the effects of instructing caregivers to use specific communication strategies and the impact of the overall use of such strategies on children's communication outcomes and general functioning. The research also set out to examine verbal and nonverbal communication bids by caregivers when interacting with children with autism. The aim was to determine whether bids that were declarative were more successful at facilitating rate of child responding during interactions, compared to imperative bids for communication. As well as determining the rate of responding, the quality of the child response (responsiveness) was also determined as measured through experience sharing.

Methods:

A non-equivalent groups quasi-experimental design, with two experimental and one comparison (control) group with pre-test and

post-test measures, was used to demonstrate the feasibility of implementing a relationship-focused model, with detailed documentation of group treatment effects and individual results. Analyses of changes in pre and post-test measures were conducted for children and caregivers. A total of 16 children on the autism spectrum, aged between 3.9 and 8 years were involved in the project. The study examined the effects of instructing caregivers to communicate to invite experience-sharing by increasing their frequency of declarative communication initiations. A comparison group received the usual program provided at the centre. The ratios of imperative to declarative communication bids of the care-givers were measured pre and post intervention, as were child social responsiveness, communication skills, adaptive functioning and measures of parental stress and coping.

Results:

Descriptive statistics were used to present the results where outcome measures were analysed to measure change and to assess the benefits of the intervention. Findings suggest that parents and staff were able to successfully modify their communication in the desired declarative manner, as evidenced by video-recorded play sessions. Furthermore, adult communicative adaptation appeared to correspond with increased child responsiveness. Other measures conducted at post-test, showed variable results, supporting the need for larger, controlled, longitudinal studies.

Conclusions:

Promoting positive caregiver and child interactions, and the implications of such exchanges, provide valuable insights. There is a compelling argument for consideration of the impact of adult communication and interactional style on the ability to influence the types of communicative functions used by children with autism. If caregivers are taught to adapt their communication style with the child with autism so that they use more declarative communication, they are likely to facilitate aspects of social-communicative development.

L. A. Vismara², A. L. Fitzpatrick¹, J. Winter¹, J. G. Greenson¹, M. L. Rocha³, G. Dawson⁴, C. Lord⁵ and S. J. Rogers⁶,
(1)University of Washington, (2)University of California at Davis MIND Institute, (3)UC Davis MIND Institute, (4)Autism Speaks, UNC Chapel Hill, (5)Weill Cornell Medical College, (6)MIND Institute; University of California at Davis

Background: Early intervention, begun before age 2, has demonstrated efficacy in improving outcomes for children with ASD (Dawson et al., 2010). However, the impact of early autism intervention on caregivers is not yet well understood. Previous research has consistently demonstrated that parents of children with ASD have increased stress levels, but innovations in autism intervention are needed to address this issue and help parents maintain and increase their psychological well-being, even after an ASD diagnosis.

Objectives: This study is designed to examine the impact of an intervention based on the Early Start Denver Model (ESDM) on parenting-related stress and parent sense of competence. We hypothesize that parents in the ESDM group will demonstrate increased sense of competence and decreased parenting-related stress compared with parents who receive community intervention as usual (Community).

Methods: Ninety seven parents of children with ASD from three different communities in the United States participated in a randomized, controlled trial of the ESDM. Children were diagnosed and began the study at 12-24 months of age. In phase 1, the ESDM group received three months of parent coaching. In phase 2, the ESDM group received 2 years of intensive, in-home, therapist- and parent-delivered intervention. The Community group obtained intervention from community providers over these same time periods. Parents in both groups were assessed for parenting-related stress and sense of competence through self-report questionnaires at the same four, longitudinal time points.

Results: During phase 1, the parents whose children received ESDM reported no increase in parenting-related stress, whereas parents in the Community group experienced increased parenting-related stress. Parental sense of competence did not differ between groups during phase 1. As required by our Data Safety and

Monitoring Board, data for phase 2 will be analyzed by an independent data coordinating center after all participants have completed phase 2 of the study (December, 2012). At that time, we will examine whether parents in the ESDM group 1) maintain lower stress levels and 2) experience an enhanced sense of competence after Year 1 and Year 2 of intensive, in-home, therapist-delivered intervention. We will use General Estimating Equations to evaluate the associations of group assignment on parenting stress and sense of competence at one- and two-years of follow up of the study adjusting for potential confounders as needed.

Conclusions: Phase 1 results suggest that a parent-coaching intervention designed for parents to implement with their young children may help maintain parental adjustment after a child is newly diagnosed with ASD and while parents are learning a new intervention. Future analyses will determine whether, in phase 2, parents in the ESDM group maintain or decrease stress levels and demonstrate an increased sense of competence, compared with the Community group. The goal is to provide a manualized, naturalistic, approach to intervention for very young children that also supports parental adjustment to the increased demands of early autism intervention.

143.127 127 Social Functioning and Parental Well-Being in Preschoolers with ASD. A. M. Rowley*¹, D. Coman², A. Gutierrez³ and M. Alessandri², (1)*Nova Southeastern University*, (2)*University of Miami*, (3)*Florida International University*

Background: Families of children with autism spectrum disorders (ASD) experience greater stress levels than families with other or no disabilities, placing them at risk for poor mental health (Boyd, 2002). Research suggests parental distress may be related to child functioning areas across several domains, including autism severity and cognitive ability (Lounds et al., 2007). Similarly, maternal stress has been associated with treatment outcome for children with ASD (Robbins, Dunlap, & Plienis, 1991). The primary intervention for most children with autism is the education they receive in school. Given the importance of early school-based interventions for these children (Dawson et al., 2010), and the important role parents play in their child's response to treatment, it is critical to understand

which domains of functioning may significantly impact parental distress and well-being (Taylor & Warren, 2012).

Objectives: To examine the effects of social and autism severity outcomes in preschoolers enrolled in TEACCH, LEAP, and Business as Usual (BAU) classrooms on parental stress and depression. We hypothesized that reports of lower social functioning in children would be associated with increased parental stress and depression.

Methods: Participants included 198 preschoolers with a confirmed ASD diagnosis and their parents. Students were aged 34 to 62 months ($M = 47.60$, $SD = 7.49$) and enrolled into high fidelity TEACCH ($n = 85$), LEAP ($n = 54$), or BAU ($n = 59$) classrooms. Students were administered the *Autism Diagnostic Observation Schedule*. Parents completed the *Social Communication Questionnaire*, the *Social Responsiveness Scale*, the *Beck Depression Inventory-II*, and the *Parenting Stress Index-SF*.

Results: Controlling for age, symptom severity, and pre-assessment scores, results indicated end of the school year parent reports of their child's social functioning as they relate to social awareness, $R^2 = .49$, $F(4, 150) = 11.44$, $p < .001$, $\beta = 0.36$, $t(150) = 3.65$, $p < .001$, social cognition, $R^2 = 0.49$, $F(4, 148) = 11.48$, $p < .001$, $\beta = 0.51$, $t(148) = 4.72$, $p < .001$, social communication, $R^2 = 0.53$, $F(4, 150) = 14.03$, $p < .001$, $\beta = 0.47$, $t(150) = 4.69$, $p < .001$, and social motivation, $R^2 = 0.44$, $F(4, 150) = 8.59$, $p < .001$, $\beta = 0.33$, $t(150) = 3.07$, $p < .01$ were associated with self-reports of distress. Additionally, autistic mannerisms was shown to be associated with self-reports of distress, $R^2 = 0.52$, $F(4, 150) = 13.49$, $p < .001$, $\beta = 0.43$, $t(150) = 4.47$, $p < .001$, and symptoms of depression, $R^2 = 0.30$, $F(4, 147) = 3.46$, $p < .05$, $\beta = 0.27$, $t(147) = 2.51$, $p < .05$.

Conclusions: Results from the current study suggest a relationship between student improvements and parental distress at the end of the school year. Parental reports of their child's level of social functioning at the end of the school year were associated with self-reported stress levels and depressive symptomatology. Specifically, lower levels of functioning were

associated with higher stress as well as some associations with depression.

143.128 128 Parent-Mediated Intervention to Improve the Perceptions of Mothers of Children with Autism Spectrum Disorder. A. Gerber*¹, M. Siller¹, T. Hutman² and M. Sigman², (1)*Hunter College of the City University of New York*, (2)*University of California, Los Angeles*

Background: Several recent clinical trials of parent-mediated interventions for children with autism spectrum disorder (ASD) have demonstrated improvements in responsive parental behaviors, child communication and autism symptom severity (Kasari et al., 2010; Aldred, et al, 2004; Siller et. al, 2012; Green et al, 2010; Carter et al., 2011). Little is known, however, about the effects of these interventions on the parents' cognitions and emotions.

Objectives: The current study is a randomized clinical trial of Focused Playtime Intervention (FPI), a parent-mediated intervention that has been shown to effectively improve responsive parental behaviors and, to some extent, child communication (Siller et al., 2012). Treatment effects on parent cognitions and emotions were evaluated using a battery of parent-report questionnaires.

Methods: The sample included 70 mothers of children with ASD. Children ranged in age from 32-82 months ($M=57.1$ months, $SD=12.3$) and showed limited expressive language skills ($M=15.9$ months, $SD=9.0$) on the Mullen Scales of Early Learning (MSEL; Mullen, 1995). Upon intake, families were randomly assigned to either the control or experimental group. Parents in both groups participated in four educational sessions on advocating effectively for a young child with ASD. In addition, parents and children assigned to the experimental group were invited to participate in 12 in-home sessions of FPI. Maternal cognitions and emotions were evaluated before and after the 4-month treatment period, as well as 12 months thereafter, using three questionnaire measures: (1) The Questionnaire on Resources and Stress (QRS; Konstantareas, Homatidis & Plowright, 1992); (2) the Maternal Perception of Child Attachment questionnaire (MPCA; Hoppes & Harris, 1990); and (3) the Concepts of Development Questionnaire (CODQ; Sameroff & Feil, 1985). Over the course of the study, we observed a fairly low attrition rate of 11%.

Questionnaire data, however, were missing for 8%, 20%, and 40% of the participants at baseline, exit, and follow-up, respectively.

Results: Residual gain scores were calculated to represent change on parent measures between the three time points (intake, exit, and follow up). Analysis indicated that between intake and exit, mothers in the experimental group ($M = 0.10$, $SE = 0.07$) showed larger gains in perceived child attachment (MPCA) than mothers in the control group ($M = -0.13$, $SE = 0.07$), $t(51) = 2.36$, $p < .05$. Mothers in the experimental group ($M = 0.09$, $SE = 0.06$) also demonstrated greater gains in their understanding of child development (Perspectivistic subscale of CODQ) than mothers in the control group ($M = -0.07$, $SE = 0.04$), between intake and follow up, $t(29.20) = 2.12$, $p < .05$. Treatment effects on parent-reported stress (QRS) were not significant.

Conclusions: Results from this study reveal significant treatment gains in mothers' perception of child attachment and understanding of child development, but not in the parents' level of reported stress. One limitation of the current study is the modest amount of missing data. To address this limitation, future analyses will utilize multiple imputation to increase statistical power and prevent erroneous conclusions (Enders, 2010).

143.129 129 Does Broader Autism Phenotype in Mothers Affect Their Child's Degree of Progress Following Parent-Mediated Intervention?. S. Wigham¹, L. Gray², A. S. Le Couteur², H. McConachie² and J. Parr*³, (1)*Newcastle University Institute of Health and Society*, (2)*Newcastle University*, (3)*Institute of Neuroscience, Newcastle University*

Background: Parent-mediated early intervention improves parent-child dyadic social communication between children with ASD and their parents (Green et al., and the PACT Consortium, 2010). However, some parents of children with ASD show ASD-type traits and behaviours – the Broader Autism Phenotype (BAP). Potentially, parental BAP might impact upon parent child interaction, and thus the delivery and effectiveness of parent-mediated intervention (Parr et al., 2011).

Objectives: We aimed to investigate the relationship between mothers' BAP traits and behaviours, and 1. change in mother-child

interaction, and 2. their child's progress following parent-mediated intervention.

Methods: Family History Subject Interviews (FHI) (Parr et al., and the IMGSA) were undertaken during a study investigating the reliability of the FHI when administered by telephone. Interviews were undertaken with 19 mothers from a Newcastle intervention study, in which archive data were also available on change in mother-child interaction strategies, and children's developmental progress following intervention (McConachie et al., 2005).

Results: There was a significant negative correlation between BAP total scores and mother-child interaction. At an individual level, there was less change in mother-child interaction scores for mothers who scored 2 or above on the BAP factor item total score. In addition, the children of mothers who scored 2 or above on the BAP total score showed less change in their expressive and receptive language scores following intervention.

Conclusions: In this pilot and feasibility study, mothers with more BAP behaviours and traits showed less improvement in interaction with their child with ASD, and their children made less developmental progress. This finding potentially has implications for parent-mediated intervention for children with ASD. The influence of the BAP on parent-child interaction will now be measured in the Preschool Autism Communication Trial follow up study (commencing Spring 2013), as part of an investigation into the moderators of effective intervention, and the need to better understand how interventions should be individualised for particular children and families.

143.130 130 Effect of Parent Expectancies of CHILD Therapy On Perceived Therapy Outcomes in Children with Autism Spectrum Disorder. A. Dammann*, K. Tang and J. J. Diehl, *University of Notre Dame*

Background: Previous research on client expectations has shown that a client will report greater therapy outcomes when there are higher expectations at the start of treatment (Dew & Bickman, 2005). One explanation for this association is through expectancy effects; that is, a client who believes they will see a better outcome at the conclusion of therapy often will see better treatment outcomes (Barker, Funk, & Houston, 1988). Research on this effect has

primarily looked at adults' expectancies of their own psychotherapy for generalized anxiety disorder and depression. However, it is unclear if expectancy effects also occur in child therapy, specifically in therapy for children with autism spectrum disorder (ASD). In therapy for children with ASD, parents are essential for the continuity, maintenance, and generalization of learned skills. Therefore, we wanted to see if parents' expectations of therapy for their child with ASD (via expectancy effects) would be associated with greater parent-reported treatment outcomes at the end of therapy.

Objectives: This study looked at whether parents' expectations of the outcome of child therapy would be related to their perception of the child's progress in therapy. We predicted that higher parent expectations at the start of therapy would lead to greater parent-reported child progress at the end of the therapy.

Methods: Participants were parents of 15 children participating in a study that used an interactive humanoid robot in addition to a therapist to teach social skills to children with ASD in Applied Behavior Analysis therapy. Parents were given an adapted version of the Credibility/Expectancy Questionnaire (CEQ; Devilly & Borkovec, 2000) prior to therapy, after the middle session, at the end of therapy, and at the three-month follow-up. Parents recorded their child's frequency of displayed social skills in the home environment through a social behavior tracking sheet measured over three days prior to therapy, after every two sessions, at the end of therapy, and at the three-month follow-up. A percent increase or decrease in social skills was calculated from the earliest to the latest available tracking sheet from each parent and was compared to the percent increase in social skills the parents expected to see, as reported through the CEQ prior to therapy.

Results: Using Spearman's Rank Order Correlation, parents' expectations of the outcome of therapy were significantly related to the progress they reported seeing in their child at the end of therapy ($\rho = .765, p < .001$). This suggests that higher parent expectations are related to parent-reported improvement in social skills from the start to the end of therapy. In-session data are currently being analyzed and will also be considered in relation to parent expectations.

Conclusions: These data suggest that expectancy effects are held not just by the client in therapy but are also manifested by parents of children with ASD in therapy. Expectations held by a parent have a significant influence on the subjective progress they observe in their child during therapy. Further research should examine the effect these expectations have on the objective measure of their child's outcome in therapy.

143.131 131 Measuring Sociodemographic Risk in Families of Very Young Children Receiving Early Autism Intervention. J. Winter¹, A. Estes¹, Z. Zargar*¹, J. G. Greenson¹, M. L. Rocha², L. A. Vismara³, A. L. Fitzpatrick¹ and S. J. Rogers⁴,
(1)University of Washington, (2)UC Davis MIND Institute,
(3)University of California at Davis MIND Institute,
(4)University of California Davis Medical Center

Background: Research has demonstrated that early intervention for young children with autism has a significant positive impact on child progress (Dawson et al., 2010). However, little is known about the effectiveness of early autism intervention for children with different levels of sociodemographic risk. The developmental systems model describes a process by which risk factors, including family sociodemographic factors, act to disrupt central family functions, and can negatively or positively influence the effectiveness of early intervention (Guralnick, 2001). We will examine the effect of these family risk factors on the efficacy of the Early Start Denver Model (ESDM) intervention.

Objectives: We aim to develop a scale of family sociodemographic risk (SDR) factors. We will examine the relationship of this new scale to child and family factors in order to investigate the validity of this new measure. We hypothesize that families with a greater number of risk factors will have children with significantly lower communication abilities and higher levels of problem behaviors.

Methods: We created the SDR scale from existing variables in a multisite, randomized, controlled trial of early intervention using the ESDM. These data are from a subset of 74 families, when the child with autism was 12-24 months old. Items were from the Life Experiences Survey (Sarason et al., 1978), the CHARGE family characteristics questionnaire (Hertz-Picciotto et al., 2006), and enrollment interviews. The scale

consisted of 16 risk factors. For each factor endorsed by the parent, a point was given, for a possible score of 16 points.

Results: Item-level analysis of SDR revealed the following: child not living with both parents, 10.8%, mother with high school degree or less, 16.2%, father with high school degree or less, 10.8%, unemployed father 6.8%, family income below \$50,000, 23%, one/both parents born outside the US, 21.6% resided in US for < 10 years, 17.6%, one/both parents with a primary language other than English, 25.7%, sibling with a disability, 29.7%, mother/ father with a disability, 13.5%, parent with a recent major illness, 13.5%, parent in jail, 2.7%, recent foreclosure, 5.4%, recently moved, 24.3%, recent pregnancy, 12.2%, recent death in family, 13.5%. The responses ranged from 0-9 points (mean = 2.47, SD = 1.753, median = 2, mode = 2). Of the respondents, 10.8% had a score of 0, 18.9% had a score of 1, 25.7% had a score of 2, 23% had a score of 3, 10.8% had a score of 4, 6.8% had a score of 5, and scores of 7, 8, and 9 were found in 1.4% of children each. Additional analyses addressing validity will be presented, including the relationship of the SDR score to child communication, problem behaviors and other family characteristics.

Conclusions: The results suggest that the SDR scale may be a useful tool to investigate variability in response to intervention and parent learning. These family risk factors may have implications for individualization of intervention and ultimately increase the effectiveness of support for parents in the context of early autism intervention.

143.132 132 The Autism Course for Spouses Is an Effective Training Program. E. M. Blijd-Hoogewys*¹ and A. Talboom²,
(1)Lentis, (2)MEE Drenthe

Background:

The autism symptoms – the persistent deficits in social interaction and communication, and the restricted, repetitive patterns of behavior and interests - not only lead to problems in adults with Autism Spectrum Disorders (ASD) but can also have a major impact on their potential romantic relationships. The Autism Course for Spouses is developed to help women of men with ASD. Since, there are also men without an official ASD

diagnosis – f.i. because a husband does not see the need to look for such a diagnosis - the course is also accessible to spouses of men with presumable ASD.

The aim of the Autism Course for Spouses is fourfold: receiving psycho-education on autism, gaining insight in the effects of autism on the partner relationship, receiving tips to improve the communication with the autistic man, and stimulating the empowerment of the spouse. In doing so, the focus in the course is more oriented towards strengths - of both the spouse and her autistic partner - than (only) towards shortcomings.

The Autism Course for Spouses contains ten sessions, taking place every other week, each taking two hours. There are eight to ten participants and two therapists. Each session has a specific theme. The order of the themes is fixed.

Objectives:

The objective of this study was to test whether the Autism Course for Spouses is effective.

Methods:

In total, N=88 spouses (M=49 years old, M=23 years of relationship, M=2.4 children), of husbands with ASD are included in this study.

Prior to the course, a semi-structured interview is conducted with each spouse: in order to check whether autism symptoms are reasonably present in the husband (measured indirectly) and whether the spouse concerned would fit in the Autism Course for Spouses.

Next to that, all spouses filled in questionnaires prior to the course, right after completion of the course and at follow-up (3 months later). The following (Dutch) questionnaires were used AQ (Autism Questionnaire, version for spouses), visual analogue scales (concerning relationship issues), UCL (coping), SCL-90 (multi-dimensional list of complaints) and Rosenberg (self-esteem).

Results:

Concerning the husband with (presumable) ASD: 38% had an official ASD diagnosis at the beginning, 87% had an AQ score indicative for ASD. It should be noted, that the cut-off score of this questionnaire is set for adults with an autistic disorder or Asperger's disorder; PDD-NOS is not included.

Research shows that the women reported significant improvements right after completion of the course: concerning the interaction with their husbands (Chi Square, $p < .05$), their coping style (paired sample T-test, $p < .01$), their general wellbeing, psychiatric symptoms in general and specifically concerning depression, anxiety, somatic complaints, insufficiency and distrust (Wilcoxon Signed Rank Test, $p < .05$), and self-esteem (paired sample T-test, $p < .05$). At follow-up, self-esteem has improved even more ($p = .05$).

Conclusions:

The Autism Course for Spouses is an effective training program.

143.133 133 The Importance of the Quality of the Coparenting Partnership in Predicting Parenting Stress in Parents of Children with an ASD. C. D. May*¹, R. Fletcher², I. Dempsey² and L. Newman³, (1)*University of Newcastle*, (2)*University of Newcastle*, (3)*Monash University*

Background:

Many studies have demonstrated that parents of children with an ASD experience high levels of Parenting Stress and that high levels of Parenting Stress predict poor child and family outcomes. Coparenting theory and research indicates that the quality of the Coparenting Partnership is predictive of parenting stress; can be influenced through intervention; is associated with child and parent outcomes; and that this association may be stronger in families facing a high degree of parenting difficulty. However, little is known about the importance of the Coparenting Partnership in families where there is a child with an ASD.

Objectives:

This study aimed to explore the relationship between the Coparenting Partnership and Parenting Stress in biological cohabitating parenting couples with a young child with an ASD.

Methods:

This study employed a mixed, sequential methodology to explore the relationship between the Coparenting Partnership and Parenting Stress in cohabitating biological mothers (N=79) and fathers (N=72) of children with an ASD. A subsequent qualitative study, using semi-structured interviews, explored the adaptation of the Coparenting Partnership to the parenting of a child with an ASD in mothers (N=11) and fathers (N=11) from the same cohort.

Parental perceptions of the quality of their Coparenting Partnership, Autism Specific Parenting Self-efficacy (ASPSE), Family Support, and Parenting Stress were assessed with validated scales such as the Parenting Alliance Measure and the Parenting Stress Index. Severity of ASD and socioeconomic data was also collected. Subjects were recruited through autism specific schools and other sources in the metropolitan centres of NSW, Australia. Quantitative data was analysed with SPSS & AMOS. Interviews were thematically analysed with the support of NVIVO software.

Results:

Parents relied more heavily on their parenting partner than any other source of support. The Coparenting Partnership demonstrated a stronger correlation with Parenting Stress than any other variable (Father: $r = .512, p < .001$, Mother: $r = .357, p = .001$) and a stronger relationship with Parenting Stress than previously demonstrated in normative samples. Other factors, such as family support & socioeconomic position demonstrated weak relationships with Parenting Stress. Structural Equation Modelling supported the existence of a causal pathway from ASPSE to Parenting Stress which is mediated by the quality of the Coparenting Partnership.

The emergence of the child's ASD caused parents to alter roles and responsibilities in their parenting partnerships. Fathers and mothers often had different parenting experiences and often had different roles however, parents valued this difference and worked together to promote their coparenting competence. Parents spoke about the importance of a sense of shared parenting endeavour and described how their parenting self-

efficacy relied on the quality of their Coparenting Partnership.

Conclusions:

The quality of the Coparenting Partnership is an important predictor of Parenting Stress in families where there is a child with an ASD. Children with an ASD are likely to benefit from the development of practices that enhance and strengthen their parent's Coparenting Partnerships. Intervention may be particularly effective in the early stages of the family's transition to the parenting of a child with an ASD.

143.134 134 Parent-Led Intervention Method to Increase Eye Contact Initiation in Young Children with Autism Spectrum Disorder. M. Muuvila*¹, J. K. Hietanen², K. Eriksson³ and A. Kylliäinen², (1)Child Psychiatry Unit, Tampere University Hospital, (2)University of Tampere, (3)Tampere University Hospital

Background: Difficulties in eye contact are well recognised in children with autism spectrum disorder (ASD). Reduced interest towards another person's face and eyes may contribute to the abnormalities in social development of children with ASD, in general. Therefore, it is important to motivate them towards other people's eyes and faces as early as possible. Recent interventions for children with ASD have, indeed, focused on the development of early non-verbal social communication skills. Interestingly, some recent studies have shown that imitating the behaviour of children with ASD improves their gaze behaviour and social initiations. In addition, involvement of parents in interventions has been shown to reduce parental stress and improve parent-child interaction. However, only a few studies have investigated the efficacy of parent-led intervention methods for young children with ASD.

Objectives: The aim is to plan and test a parent-led intervention method targeted to increase eye contact initiation in young children with ASD. The suggested intervention method is intended as additional to the treatment as usual (TAU). It is predicted that children's motivation towards faces will increase if initiation of eye contact is reinforced by trying to make it rewarding. It is further assumed that improvements in children's social communication will reflect positively to the

parent-child interaction and parents' image of their child.

Methods: The suitability of the intervention method was first tested in a family with a 4-year-old boy with ASD. In an ongoing study, 20 newly diagnosed, 3 to 4-year-old children with ASD are randomly divided into two groups. In the first group, parents are taught and encouraged to do daily eye contact exercises with their child in addition to TAU. The second group receives only TAU. The daily exercises include encouraging the child to use eye contact for requesting food and physical contact, and imitation of the child's actions in a specific manner. This intervention will last for 5 months and the progress will be monitored through follow-up assessments and phone-calls. Baseline and outcome measures are based, among others, on observations of gaze behaviour during parent-child interaction and questionnaires tapping on parents' experiences.

Results: The preliminary results from testing the method suggest that relatively simple exercises attached to predictable daily routines are suitable to be carried out in the daily lives of the families. Moreover, in the pilot family, imitation of the child's actions seemed to increase his initiations towards the imitating parent.

Conclusions: Evidence-based, parent-led intervention methods for young children with ASD are needed. It is expected that this study will help to introduce new evidence-based methods for autism-focused intervention and provide guidelines for supporting gaze behaviour, and social skills in general, in children with ASD.

Cognition and Behavior Program

144 Cognition and Behavior II - Cognition

144.135 135 An Empirical Analysis of the BASC Executive Function Content Scale with Individuals with ASD. E. Gardiner¹, S. M. Hutchison², K. Kerns² and G. Iarocci*¹, (1)*Simon Fraser University*, (2)*University of Victoria*

Background: Executive Functions (EF) refer to higher cognitive processes involved in the conscious control of thought and action. Behavior scales are used to better understand EF deficits among clinical populations. The Behavior Assessment System for Children 2nd ed.–Parent Rating Scale (BASC-2 PRS; Reynolds & Kamphaus, 2004), contains a supplemental index

called the Executive Function content scale (EFCS), which is useful for assessing EF (Reynolds & Kamphaus, 2002). Sullivan and Riccio (2006) found that participants with ADHD and other clinical diagnoses were rated as exhibiting significantly higher executive dysfunction behaviors. However, it is not known if the EFCS is appropriate for use with the ASD population.

Objectives: 1) To compare EFCS scores between children with ASD and those without ASD (typically developing; TD); and 2) to examine how EFCS scores correlate with computer-based EF measures in a subset of preschool-aged children.

Methods: One hundred and fifty children (ASD=80; TD=70), matched on chronological age (range=3-18 years, $M=9.76$), were rated by their parents using the BASC-2 PRS.

A subset of thirty-five age- and IQ-matched children (ASD=15; TD=20), 3-6 years old, were also administered an EF battery consisting of computer-based measures of inhibition (e.g., Boy-girl Stroop), planning (Tower of Hanoi), and working memory (Self-ordered Search; Kerns & McInerney, 2007). We predicted that EFCS scores would be associated with performance-based measures of EF; however, specific predictions were not made, as this aspect of the study was exploratory.

Results: Overall, participants with ASD had significantly higher EFCS scores than TD participants, $F(1)=41.23$, $p=.00$, indicating that the parents of the children and adolescents with ASD reported higher levels of executive dysfunction. This finding was not related to EF difficulties in individuals with ASD developing over time (Yerys et al., 2007), as the interaction between age group and diagnosis was not significant $F(4)=1.58$, $p>.10$. Moreover, in our subset ($n=35$) of children aged 3-6 years, EFCS score differences were also significant, $t(33)=2.69$, $p<.05$, indicating that participants with ASD demonstrated greater executive dysfunction, even at this young age.

Correlational analyses among EFCS scores and EF performance within the subset ($n=35$) revealed that for children with ASD, EFCS scores were significantly associated ($p<.01$) with performance

on the Stroop task, such that better performance was associated with less executive dysfunction.

Conclusions: We found that participants with ASD had significantly higher EFCS scores than TD participants, indicating greater overall executive dysfunction for the former group. These findings are consistent with those of Sullivan & Riccio (2006), and suggest that the EFCS scale has clinical utility for detecting EF difficulties in the ASD population as early as the preschool years.

With regard to the relations between EFCS scores and performance-based measures of EF, the findings indicate that the EFCS is measuring an aspect of EF that differs from traditional performance-based tasks that investigate EF in a componential way (i.e., inhibition, working memory, and planning). As the EFCS is taken from a measure of day-to-day adaptive functioning, examining EF in this way provides supplementary information from the unique perspective of the parent.

144.136 136 An Eye-Tracking Study of Visual Attention to Human and Nonhuman Animals, Landscapes and Abstract Patterns in Young Children with Autism Spectrum Disorder. D. Plesa Skwerer*, *Boston University*

Background: Studies of visual attention deployment using eye-tracking methods have suggested various atypicalities in the gaze behavior of individuals with autism spectrum disorder (ASD), in particular in response to social stimuli, but empirical evidence that visual preferences reflect the social profile characteristic of the disorder remains controversial (Klin et al., 2002; van der Geest et al., 2002; Boraston & Blakemore, 2007)

. Research on the gaze behavior of human infants has demonstrated a preference for attractive human faces even in newborns, indicative of a possibly innate biasing mechanism toward social engagement, although recent findings have suggested that this preference extends beyond conspecifics in 3- 4 month olds (Quinn, Kelly, Lee, Pascalis, & Slater, 2008). Currently little is known about the early development of visual preferences in children with ASD, who show deficits in face processing and in social reciprocity that may be linked to abnormalities in social attention (e.g. limited attentional bias for faces and avoidance of eye-contact).

Objectives: The goal of this study was to investigate whether and how children with ASD differ from typically-developing (TD) children in their visual preferences for several categories of visual stimuli, besides human faces and objects, which have been the focus of prior research. Specifically, we examined whether children with ASD show content-related visual attention deployment differences compared to TD children of the same mental age, and whether attentional biases or visual preferences reflect the *early* social phenotypes of the ASD group.

Methods: Twenty-seven children with ASD (ages 3-6 years) and 35 TD children in the same age range passively viewed a slide-show of 50 image-pairs presented on a TOBII 1750 eye-tracker. Images of people (adults, children, babies), paired with images of nonhuman animals, flowers, landscapes, or abstract designs were displayed side-by-side for 6 seconds, separated by a 1-second central fixation stimulus. The image pairs were matched for complexity, mean luminance and balanced (left-right) for content categories.

Results: Eye-tracking data provided evidence of group differences on several measures of content-related eye-movements. An ANOVA comparing groups on total fixation times to the 6 content categories (people, animals, landscapes, flowers, butterflies and abstract images) revealed a significant category effect ($F(5,58) = 32.3, p < .001$) and a significant group by category interaction ($F(5,68) = 6.42, p = .011$). TD children showed a preference for images of people over all other image-categories, whereas children with ASD showed no difference in total fixation durations between nonhuman animals, humans and abstract patterns.

Conclusions:

Differences between the TD and ASD children in patterns of spontaneous viewing behavior and visual preferences found in this study suggest that preferential attention deployment may account for aspects of the ASD social phenotype. Findings will be discussed in terms of the significance of investigating gaze behavior as an index of social attention and preferences in children with ASD.

144.137 137 Assessing the Perceptual Origins of Cognitive Peaks in Autism. V. M. Doobay*¹, V. A. Bao¹, D. Tullo¹, L. Mottron²

and A. Bertone², (1)Perceptual Neuroscience Laboratory for Autism and Development (PNLab), (2)Centre d'excellence en Troubles envahissants du développement de l'Université de Montréal (CETEDUM)

Background: Individuals with autism recurrently demonstrate better performance on visuo-spatial cognitive tasks (referred to as cognitive peaks), as exemplified by superior performance on the Block Design Task (BDT) subtest of the Wechsler Intelligence Scale (Caron et al, 2006). Cognitive accounts suggest that peak BDT performance derives from a reduced "top-down" interference of perceptual cohesiveness of the global figure. Whereas, perceptual accounts suggest that peaks may originate from superior local visual processing (bottom-up) of component blocks (Shah & Frith, 1993). The latter hypothesis is based off of differential sensitivity to low-level, elementary information characterized by luminance (increased sensitivity) or texture-defined (decreased sensitivity) visual attributes (Bertone et al, 2005; Vandenbrouke et al, 2008). If manipulating visual attributes, of the BDT, differentially affects autistic performance, it can then be argued that superior visuo-cognitive abilities in autism may have a partially perceptual origin.

Objectives: To demonstrate the relative role of bottom-up and top down-processes in visuo-spatial peaks in autism by assessing whether performance on a computerized, reversed BDT is differentially affected by manipulating the visual attributes of its component blocks.

Methods: 10 participants with autism and 10 typically developing participants, matched for age and full-scale Wechsler IQ, were asked to complete a computerized reversed BDT (Caron et al, 2006). In addition to obtaining comparable performance relative to the traditional BDT, using a computerized reversed BDT allowed for precise manipulation of physical block characteristics defining the chosen visual attribute conditions. Trials consisted of a target block design with a matrix size of either 4 x 4, 9 x 9, or 16 x 16 presented at the center of a touch-sensitive screen, with four possible probes (one matching the target) presented simultaneously around it. Participants were asked to touch the matching probe as quickly and accurately as possible. Importantly, the visual attributes of the blocks were manipulated across these three matrix sizes,

defined by either (a) traditional red/white surfaces, (b) luminance-defined (high-contrast) black/white surfaces, or (c) texture-defined surfaces. In addition, the perceptual coherence of block designs was also manipulated by varying the number of 'adjacencies' of opposite-colored edges. The low-coherence (LC) designs necessitated increased local analysis to be resolved (block-by-block-processing), relative to high-coherence (HC) designs. Reaction times (RTs) for both groups were measured across all experimental conditions.

Results: On average, mean RTs for both autism and control groups were lower and comparable for HC conditions across visual attribute and matrix size conditions. When collapsed across matrix size, mean RTs in the LC condition were significantly lower (cognitive peak) in the autism group for luminance-defined, black/white attribute condition ($p=0.047$), and lower for the traditional red/white condition ($p=0.072$). However, group differences were not evidenced for the texture-defined condition ($p=0.19$).

Conclusions: In the present study, a cognitive peak on a reversed BDT was not manifested in the autism group when constituent blocks were defined by texture-information, a visual attribute that is less efficiently processed in autism. Such results indicate that the differential processing of low-level perceptual information may have an effect on higher-level visuo-spatial performance in autism.

144.138 138 Attention Deficits On the Continuous Performance Test in Youths with Autism Spectrum Disorders and Their Unaffected Siblings. Y. L. Chien* and S. S. F. Gau, *National Taiwan University Hospital*

Background: Autism is a neurodevelopmental disorder with characteristic neuropsychological functioning. Evidence supports executive dysfunction in individuals with autism, but results regarding attention deficit were inconsistent across studies. Little is known about the attention in unaffected siblings of probands with ASD and differential attention capacity between autistic disorder and Asperger's disorder.

Objectives: This study aimed to compare the attention capacity of probands with autism spectrum disorders (ASDs, including autistic

disorder and Asperger's disorder), their unaffected siblings, and typically developing youths.

Methods: We assessed 354 probands, aged 10.96 ± 3.15 (male, 90%), diagnosed with autistic disorder ($n = 216$) or Asperger's disorder ($n = 138$) according to the DSM-IV criteria, 287 unaffected siblings, and 255 typically developing youths (aged 11.78 ± 2.25 ; male 80%) using the Continuous Performance Test (CPT) and a questionnaire for symptoms of attention-deficit hyperactivity disorder (ADHD). Generalized linear model was used to compare the CPT performance and ADHD symptoms among probands with autism, probands with Asperger's disorder, and typically developing youths. A mixed model was applied to compare the probands with ASDs, unaffected siblings, and typically developing youths.

Results: Probands with ASDs had more omission errors, perseverative response, greater reaction time (RT), and RT standard deviation than typically developing children. The significance remained after adjusting for age and sex. The severity of ADHD and ASD symptoms was significantly associated with impaired CPT performance in probands with ASD. Probands with ASD had significantly more ADHD symptoms than unaffected siblings and typically developing children. Unaffected siblings had significantly higher RT standard deviation and variability than typically developing youths.

Conclusions: Our findings support impaired focused attention and vigilance in youths with ASDs, particularly those with autistic disorder. Although unaffected siblings did not show more severe ADHD symptoms, they had impaired focused attention assessed by the CPT. This finding implies that impaired focused attention may serve as one of potential endophenotypes for genetic studies in ASDs.

144.139 139 Attention to Social and Mechanical Objects in Relation to Autism Traits and Social Anxiety. J. Black*, C. Ashwin and M. Brosnan, *University of Bath*

Background:

Individuals with autism spectrum conditions (ASC) have been found to show differences in their attention to social and non-social information

compared to typically developing controls. For example, people with ASC show reduced attention to social information such as faces; display an attentional preference for mechanical over social items; and spend less time looking at faces in natural scenes. There is also evidence these differences in attention are seen across the broader autism spectrum, and so may be evident in a subclinical population of individuals with a high degree of autism traits. ASC are frequently found to be comorbid with social anxiety, which could impact upon the allocation of attentional resources to social information given the well-established link between anxiety and attentional biases.

Objectives:

The current study looked at the relationship between traits of autism and social anxiety in a subclinical population. It further investigated whether differences in attention to social and mechanical objects were found in relation to high and low levels of autism and social anxiety traits.

Methods:

Ninety four participants (mean age = 28; 47 males and 47 females) were administered the Autism-Spectrum Quotient (AQ) as a measure of autism traits, and the Leibowitz social anxiety scale (LSAS) to index social anxiety. Participants were grouped via median splits across their total AQ and LSAS scores into Low AQ Low SAS, Low AQ High SAS, High AQ Low SAS, and High AQ High SAS. They also completed a dot probe task, which used images of faces or cars presented simultaneously with a neutral object (houses) for 200 or 500ms. The dependent measure for the experiment was Attention Bias scores towards faces and cars.

Results:

A significant positive correlation was found between autism traits and social anxiety, $r = .47$, $p < .001$. Furthermore, a Group x Stimulus x Time interaction was found with Attention Bias scores ($p < .05$), and post-hoc tests indicated that individuals with high levels of both autism traits and social anxiety showed a diminished attentional bias towards faces compared to the

other 3 groups when stimuli were presented for 200ms. No group differences in Attentional Bias scores were found for cars.

Conclusions:

Results show that the combination of high autism traits together with higher social anxiety was associated with reduced attention to faces, an effect not seen with those having high autism traits along with low social anxiety. These findings suggest social anxiety might play a key role in the attention biases to social and non-social information seen in ASC.

144.140 140 Clinical, Cognitive and Adaptive Profiles in Children and Adolescents with High-Functioning Autism Spectrum Disorders and in Their Siblings: A Comparative Study. M. Rosa¹, O. Puig Navarro², V. Valles¹, S. Lera Miguel¹, V. Sanchez² and R. Calvo Escalona^{*2}, (1)*Hospital Clinic of Barcelona*, (2)*CIBERSAM*

Background:

Family studies have shown high evidence for the genetic basis for Autism Spectrum Disorders (ASD). In this context, there is an increasing interest in the study of ASD siblings (Bishop et al., 2006). There is quite literature of social and communicative deficits in ASD siblings (Constantino, 2006) but little referred to cognitive traits. Some previous studies have shown impairments in executive functions in ASD siblings (Delorme, 2007; Hugues 1999) but others studies did not find these results (Sumiyoshi 2011, De la Marche 2012).

Objectives:

To examine the clinical, cognitive and adaptive profile of a sample of high-functioning ASD (HF-ASD) children and adolescents and their siblings compared to normal-developing children.

Methods:

25 children and adolescents with HF-ASD, 19 HF-ASD siblings (SIB) and 25 typical-developing children and adolescents (TD) were assessed. The three groups did not differ in age (HF-ASD=12.34, SD=3.05; SIB=13.45, SD=4.86, TD=12.51, SD=3.13), socioeconomic status nor IQ (HF-ASD=101.08, SD=15.90; SIB=102.88, SD=15.31,

TD=109.08, SD=11.89). HF-ASD patients and TD subjects were matched in sex. The ASD diagnosis was confirmed using the ADI-R and DSM-IV criteria. The Kiddie-SADS was administered to assess the presence of psychiatric diagnosis. Neuropsychological assessment was administered by an experienced psychologist blind to the status of the subjects (verbal memory –VM-, visual memory and visuospatial abilities –Vis-, working memory –WM-, processing speed –PS-, executive functions –EF-). A general cognitive domain (GC) was calculated as the mean of all cognitive domains. Vineland Adaptive Behavior Scale (VABS) and BRIEF were administered to evaluate real-world functioning.

Results:

SIB group showed a higher percentage of subjects with a psychiatric diagnosis than TD children (SIB: 42%, χ^2 corrected =7.434, $p=0.006$). Two siblings meet criteria for ASD and were excluded of further analyses. The other diagnoses were ADHD and Anxiety Disorders.

HF-ASD patients showed more difficulties than TD subjects in GC ($F=8.985$, $p<0.001$, post-hoc Bonferroni $p<0.001$) and in all cognitive domains but not in VM (Vis: $F=4.032$, $p=.023$, post-hoc Bonferroni $p=.036$; WM: $F=4.024$, $p=.023$, post-hoc Bonferroni $p=.020$; PS: $F=5.783$, $p=.005$, post-hoc Bonferroni $p=.007$; EF: $F=4.781$, $p=.012$, post-hoc Bonferroni $p=.018$). When compared with their siblings, HF-ASD showed more difficulties in GC ($p=0.010$) and in PS ($p=.041$), but not in VM, WM, EF and Vis. No significant differences were found between SIB and TD groups.

HF-ASD group showed more impairments than TD subjects and than SIB group in VABS ($F=25.828$, $p<0.001$, post-hoc Bonferroni $p<0.001$). They also showed impaired real-world executive functioning when compared with both TD and SIB ($F=26.070$, $p<0.001$, post-hoc Bonferroni $p<0.001$). No significant differences were found between the SIB group and the TD subjects in functioning measures.

Conclusions:

HF-ASD children showed generalized cognitive and real-world adaptive deficits. The siblings of HF-ASD participants showed a higher rate of psychiatric disorders than the control group. Cognitive assessment revealed that there were less differences between HF-ASD subjects and their siblings than between HF-ASD and TD group, although siblings did not differ significantly from TD subjects neither in cognitive domains nor real-world adaptive functioning. These preliminary results support the need of an accurate clinical evaluation of HF-ASD siblings.

144.141 141 Cognitive Non-Verbal Profile in Autism Spectrum Disorders. B. A. Silva Dias*, *PIN - Progresso Infantil*

Background: This study seeks to highlight the importance of research on early identification of Autism Spectrum Disorders (ASD), particularly in terms of their cognitive abilities, to support the intervention plan.

The existence of a nonverbal cognitive functioning pattern in ASD has been studied over the past decades. The research supports the idea that this population present, abilities above average in some non-verbal skills, such as perception and spatial visualization in attention to detail, and seem to have more difficulty with tasks that are non-verbal or that require visuospatial perception versus conceptual in nature (Kuschener, 2007).

Objectives: Comparing non-verbal cognitive profiles

Methods: It was used the application of Leiter-R (Roid; Miller 1997), an assessment to measure the nonverbal intelligence and has been regarded as particularly useful for special populations that are not easily assessed with more traditional measures, generally based on verbal skills to three samples.

The main goal is to compare the results of the three groups; Group A, 30 children with no medical diagnosis; Group B, 30 children with Development Delay and group C, 30 children with ASD, with the diagnosis based in the ADI-R (Autism Diagnostic Interview- Revised) and ADOS (Autism Diagnostic Observation Schedule) between 3 and 5 years old.

Results: The analysis results indicated that Group A and C in Leiter-R have Total IQ scores within the average and Group B below average compared to their chronological age, indicating no general difficulties on non-verbal intelligence to ASD populations.

Looking to the profiles, both Group A and B demonstrate better results on one specific subtest – Form Completion, which is exactly one of the two subtests where Group C indicates more difficulty, relatively to perceptual scanning, recognition and the ability to perceive fragmented percepts as wholes. On the other hand, ASD populations in general presents better results in subtest – Matching, representing good skills in attention to detail, ability to scan and make visual comparisons.

Conclusions: Based on these results, it was concluded that ASD in Leiter-R have Total IQ scores at average, representing an average nonverbal cognitive profile compared to their chronological age. It was also presented a discussion with issues to be explored, as to investigate in the future the unique patterns of functioning of non-verbal ASD population, which in this study shows specific difficulties in task relatively to perceptual scanning, recognition and the ability to perceive fragmented percepts as wholes as opposed to good skills in attention to detail.

The study of a unique profile could be masked by the heterogeneity of the ASD populations, suggesting the need of a division in groups of this population.

144.142 142 Environmental Influences and Neurocognitive Profile in Autism Spectrum Disorders: A Discordant Monozygotic Twin Pairs Design. C. Willfors*¹, S. Berggren¹, P. Lichtenstein², H. Anckarsäter³ and S. Bölte², (1)Department of Women's and Children's Health, Astrid Lindgren Children's Hospital, Q2:07, Center of Neurodevelopmental Disorders (KIND), Karolinska Institutet, (2)Karolinska Institutet, (3)University of Gothenburg

Background: The cognitive phenotype of Autism Spectrum Disorders (ASDs) is characterized by a detail-focused processing style. Current research suggests both hypo connectivity and enhanced perceptual functioning to account for piecemeal processing in ASD. The study of monozygotic (MZ) twin pairs discordant for ASD phenotype appears

to be a promising lead to further examine the genetic and environmental origins of cognitive alterations in ASD.

Objectives: As a part of the Roots of Autism Twin Study Sweden ("RATSS"), to examine whether i) twins with ASD and broader ASD phenotypes show increased attention to detail, as compared to typical developed twins, and ii) whether co-twins with ASD or broader ASD phenotypes present with increased attention to detail compared to their co-twins being qualitatively or quantitatively discordant for ASD or ASD traits.

Methods: In RATSS, performance in visual attention to detail is assessed with the Embedded Figures Test (EFT; child/adult version) and the Fragmented Picture Test (FPT). Seven twin pairs discordant for ASD and 11 typically developing twin pairs were included in this study. In the group of twins being discordant for ASD (N=14), the male/female ratio was 12:2, and Wechsler IQs ranged from 65 to 115 (Md=92). In the group of typically developing twins (N=22), the male/female ratio was 8:14, with an IQ range of 81 to 126 (Md=100). Mann-Whitney U and Wilcoxon Signed Rank tests were used to compare between- and within-pair scores, respectively.

Results: Between-pair analyses for FPT scores showed a trend for typically developing twin pairs to outperform ASD individuals on the FPT tasks ($Z=1.661$; $p=.051$). Consistently, within-pair analyses indicated a trend for unaffected or less affected co-twins to show superior performance on the FPT in comparison with their ASD or broader phenotype co-twin ($Z=1.364$; $p=.086$). The same statistical analyses showed no differences neither between the pairs nor in the pairs for EFT scores ($p>.1$).

Conclusions: These preliminary data indicate a link between ASD/ASD traits and visual attention to detail. The link might be influenced by non-shared environmental factors.

144.143 143 Evaluating Executive Functions As Endophenotypes of Autism Spectrum Disorders. L. Van Eylen*, J. Steyaert, E. Ceulemans, J. Wagemans and I. Noens, *University of Leuven (KU Leuven)*

Background: Autism spectrum disorders (ASD) are highly heritable, but insight in the etiology is

still limited, mainly due to considerable heterogeneity between ASD individuals. 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 influenced by one or more of the same genes that confer susceptibility to the condition. Some of the proposed criteria for good ASD endophenotypes are that they should co-occur with ASD and be expressed at a higher rate in unaffected first degree relatives of ASD probands than in the general population. Potentially interesting ASD endophenotypes are neurocognitive measures of executive functioning (EF). EF is an umbrella term for higher-order cognitive functions necessary for the regulation of thoughts and actions. We make a distinction between five domains: cognitive flexibility, inhibition, working memory, planning and generativity.

Objectives: The aim of our study is to assess which EF measures provide good endophenotype candidates for ASD.

Methods: We developed a battery of tasks measuring each EF domain as purely as possible, containing at least two tasks per domain. This battery was administered from children with ASD (n=62), their unaffected siblings (n=38) and parents (n=91), and typically developing (TD) children (n=63) and adults (n=61).

Results: Preliminary analyses comparing 48 ASD and 48 TD children matched for age, IQ and gender, show that ASD children have problems with cognitive flexibility, inhibition and working memory. Their difficulties with cognitive flexibility were expressed as more errors on switch compared to repeat trials in one flexibility task ($p < 0.01$) and a higher reaction time on switch compared to repeat trials on another task measuring flexibility ($p = 0.04$). The group differences in inhibition and working memory depended on the task. On one inhibition task ASD children made more inhibition errors (Go/No-Go task, $p = 0.03$), while on another inhibition task (flanker task) no significant group differences were found. Concerning their working memory capacities, we only observed group differences on

the most difficult working memory task ($p = 0.02$), but not on the other task. So far, no group differences in planning and generativity were found, but not all generativity tasks have yet been analyzed.

Conclusions: We have found evidence that problems with cognitive flexibility, inhibition and working memory are potentially useful ASD endophenotypes, since they co-occur with the disorder. However, we still need to evaluate whether these features are also expressed at a higher rate in their siblings and parents than in the general population. In addition, cluster analyses will be applied to evaluate whether more homogeneous ASD subgroups can be delineated based on their EF performance. At the time of the conference the results of these additional analyses will also be available.

144.144 Executive Functioning and Behavior Problems in Intellectual Disability and Autism Spectrum Disorders. E. M. Visser^{*1}, H. Berger¹, J. Prins¹, H. Schroyen Lantman - de Valk¹ and J. P. Teunisse², (1)*Radboud University Nijmegen Medical Centre*, (2)*Dr Leo Kannerhuis*

Background: Aggression and externalizing behavioral problems are frequently reported in the intellectually disabled (ID) population. These challenging behaviors are especially common among individuals with ID who have an additional Autism Spectrum Disorder (ASD) diagnosis. It is proposed that mainly individuals with ASD who are impaired in EF might be prone to display behavioral problems, since EF deficits are related to a need for sameness, lack of impulse control, and difficulty in switching.

Objectives: The aim of this study is to measure problem behavior in an ID-population with and without ASD-diagnosis and examine the role of EF-components inhibition, updating and shifting in predicting these behavioral problems.

Methods: Sixty individuals with mild to borderline ID (IQ range 50-85) of which half were diagnosed with ASD, were recruited from three residential care providers in the Netherlands. Counselors completed rating scales concerning the participants' daily functioning, thereby reporting severity of ASD-symptoms (ratinglist of DSM-IV criteria) and deficits in EF-behavior (BRIEF, BFRS). Additionally, six neuropsychological EF-tasks were administered to measure three

different EF-components; inhibition (ANT SSV, ANT ROA), shifting (WCST, CANTAB ID/ED) and updating (Fluency, Digit Span Backwards). Challenging behavior was assessed using counselor based ratings of externalizing and internalizing behavioral problems (ABCL).

Results: ASD-diagnosis proved to have a poor predictive value for behavioral problems in our sample; no significant difference was found between the ID group with ASD and the ID group without ASD on behavioral problems. The severity of ASD-symptoms did correlate with problem behavior, but this relationship was only significant for internalizing and not for externalizing problem behavior. No significant correlations were found between neuropsychological EF-measures and behavioral problems. In contrast, reported problems in daily EF-behavior were significantly related to both internalizing and externalizing behavioral problems. Strikingly though, these relationships were mainly found in the ID-group without ASD compared to the ID-group with ASD. Posthoc analyses revealed a significant difference in variance of EF-ratings between the two groups, with a lack in variance in the ID group with ASD.

Conclusions: EF-functioning was found to be more sensitive in predicting behavioral problems than ASD-diagnosis, but only if measured using counselor based EF-ratings and not when using neuropsychological EF-tasks. However, our findings suggest that counselors rate the two ID-groups in different ways; they appear to be less able to view differentiation in EF-behavior of ID-individuals with ASD as compared to individuals diagnosed with solely ID. This finding has implications for future use of EF-rating scales in research and clinical practice.

144.145 Exploring the Cognitive Underpinnings of the Autism Phenotype. V. E. Brunson^{*1}, E. Colvert¹, E. L. Woodhouse², P. F. Bolton³ and F. Happé⁴, (1)*SGDP, Institute of Psychiatry, King's College London*, (2)*King's College London*, (3)*Institute of Psychiatry, King's College London*, (4)*SGDP, IoP, King's College London*

Background: Autism Spectrum Disorders (ASD) are currently diagnosed behaviourally based on the presence of the triad of impairments; social impairments, communication impairments and restricted and repetitive behaviours and interests (RRBIs). Three key cognitive theories; a theory of mind deficit, executive dysfunction, and weak

central coherence, have been proposed to explain the triad of impairments in ASD. However, surprisingly few studies have investigated whether different cognitive profiles are related to the triad of impairments in ASD.

Objectives: To explore the strength of the relationship between performance on theory of mind, executive function and central coherence tasks, and each impairment of the triad in ASD.

Methods: Participants were drawn from a large population-based sample of adolescent twins, which selected for 111 twin pairs with at least one twin with an ASD and 79 control twin pairs. The ASD group (83% male, average age = 13.5 years) consisted of 87 individuals with a diagnosis of autism, 23 with an ASD, and 32 with a broad spectrum diagnosis (i.e., did not quite meet clinical cut-offs) to cover the complete autism spectrum. All twin pairs were administered an extensive cognitive battery to measure IQ, language ability, theory of mind ability (mentalising and false belief), executive functioning (planning, mental flexibility, mental initiation, and inhibitory control), and central coherence (local and global processing). The ASD group were behaviourally assessed for ASD symptomatology in the three symptom domains using parent report (Autism Diagnostic Interview-Revised, ADI-R) and direct observation (Autism Diagnostic Observation Schedule-Generic, ADOS-G). For the analyses, the effects of age and IQ were controlled for using regression analyses. Four composite measures of the cognitive tasks were then created based on *a priori* assumptions about the cognitive ability that each task measured; (1) theory of mind, (2) executive functioning, (3) local coherence and (4) global coherence, to reflect both aspects of central coherence. Linear regression models examined whether the composite measures individually predicted symptom severity for the three ASD symptom domains. Hierarchical regression analyses were also conducted to examine the combined contribution of the composite measures to the three ASD symptom domains.

Results: Disparate results between the ADOS-G and ADI-R were found. Theory of mind ability alone accounted for statistically significant variation in the severity of ADOS social and communication impairments. Executive function

together with local coherence, accounted for statistically significant variation in ADOS-G RRBI symptoms. In contrast, global coherence together with theory of mind ability, accounted for statistically significant variation in both ADI-R social and communication symptoms, and local coherence accounted for statistically significant variation in ADI-R RRBI symptoms.

Conclusions: The findings complement the 'fractionable' theory of ASD proposed by Happé and Ronald (2008) that different cognitive deficits/styles may explain different parts of the triad of impairments. However, the three cognitive theories did not fully account for all of the variance in ASD symptoms and therefore may be insufficient to fully explain ASD symptomatology. The cognitive underpinnings of the autism phenotype may be much more complex than a simple unidirectional relationship between cognition and behaviour.

144.146 146 Flexible Relational Processing and Visual Paired Comparison in Autism Spectrum Disorder. C. L. Thomas*, S. B. Gaigg, M. Ring 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, which is thought to be mediated by the hippocampus (Eichenbaum, 2000).

Objectives:

Hippocampal function can be assessed using a novelty preference paradigm. When presented with a single item (familiarisation phase) then after a short interval, that item is presented alongside a new item (recognition phase), hippocampally-damaged participants will tend to show a novelty preference only if the background on which the items are presented stays the same

between familiarisation and recognition (Pascalis et al., 2009). This indicates that when the background changes, the familiar stimulus is perceived as new, due to impaired relational binding. The current study hypothesises that, since the patterning of memory in ASD is consistent with impaired hippocampal function, the same pattern of results will be demonstrated here.

Methods:

20 participants with a diagnosis of ASD and 17 typically developed (TD) individuals were matched on age and full scale IQ. Replicating Pascalis et al.'s paradigm, a single item was presented on a patterned background (familiarisation phase), after which two items were presented together, one of which was the familiar stimulus, and one new item, either on the same or different background (recognition phase). Eye movements were measured using a head-mounted eye tracker.

Results:

No significant difference was found between the groups in the total length of looking time during the recognition phase (same: $t(35) = .17, p > .05$; different: $t(35) = .48, p > .05$), indicating that any differential looking behaviour relating to novelty preference cannot be explained by differences in the amount of time spent exploring the stimuli. Analysis of novelty preference showed no significant main effects of either context ($F(1,35) = 3.86, p > .05$) or group ($F(1,35) = 0.00, p > .05$), as well as no significant interaction between the two factors ($F(1,35) = .71, p > .05$). In addition to these findings, novelty preferences exhibited by each group were found to be significantly above chance in both conditions (TD group, same: $t(16) = 4.25, p < .001$; different: $t(16) = 3.30, p < .005$. ASD group, same: $t(19) = 4.20, p < .001$; different: $t(19) = 2.54, p < .05$).

Conclusions:

The findings indicate that, despite a similar patterning of memory to patients with hippocampal damage, individuals with ASD have intact hippocampal function on this task.

Alternatively, the findings may support the idea of Chalfonte & Johnson (1996), that relational binding should be viewed in terms of combinations of features of an episodically-defined event, rather than item-context associations.

144.147 147 Gender-Specific Differences in Autism Spectrum Cognitive Profiles: Wechsler Intelligence Scales Versus Raven's Progressive Matrices. E. Marcil^{*1}, V. A. Bao¹, L. Mottron², V. M. Doobay¹ and A. Bertone², (1)*Perceptual Neuroscience Laboratory for Autism and Development (PNLab)*, (2)*Centre d'excellence en Troubles envahissants du développement de l'Université de Montréal (CETEDUM)*

Background: Differences in prevalence rates suggest gender distinctions within the autism spectrum, as may cognitive profiles. Typically, versions of the Wechsler intelligence scales (WIS), with both verbal (VIQ) and performance (PIQ) subtests, have been used as a measure of autistic cognitive ability. Existing findings include that although autistic males and females share similar cognitive profiles for VIQ subtests, females perform better on the PIQ subtests Coding and Symbol Search, but significantly worse on the Block Design subtest, compared to males (Koyama et al., 2009). However, the reliability of IQ assessment of autistic intelligence using WIS has been challenged, including because VIQ subtests require typical speech comprehension and production abilities. In contrast, Raven's Progressive Matrices (RPM), an important test of fluid and general intelligence, minimizes such requirements and thus may better estimate autistic intelligence (e.g., Dawson, et al., 2007). However, there is the possibility that male and female autistics differ in their profile of WIS versus RPM performance.

Objectives: We aimed to assess whether gender-related differences in cognitive profiles in the autism spectrum depend on the type of assessment instrument used, by testing whether WIS and RPM are equivalent measures of cognitive abilities in autism spectrum females.

Methods: Cognitive profiles were drawn from the databases of two University-affiliated autism clinics in Montreal. Participants met criteria for either the specific diagnosis of autism (AUT) or Asperger syndrome (ASP) according to DSM-IV-TR criteria. All participants were aged 20 years or older at assessment and were thus tested on the

Wechsler Adult Intelligence Scale, 3rd edition (WAIS-III) as well as RPM. WIS and RPM-based cognitive profiles of 21 females (12 AUT, 9 ASP) were compared to those of 54 males (24 AUT, 30 ASP). Full-scale (FSIQ), PIQ, and VIQ, as well as raw RPM scores were averaged across AUT and ASP subgroups; mean scores for core subtests were also obtained.

Results: WIS scores were significantly higher for autism spectrum males than for females on Wechsler FSIQ ($p=0.02$) and VIQ ($p=0.03$) but not for PIQ ($p=0.79$). Gender-contingent differences on some WIS subtests were also found, with autism spectrum males outperforming females on Arithmetic ($p<0.01$) and Matrix Reasoning ($p=0.05$) subtests. When controlling for age at assessment, ANCOVAs revealed that Gender differences were not found for RPM performance ($p=0.85$).

Conclusions: Comparing WIS and RPM performance in autism spectrum males versus females provides preliminary insight into possible gender distinctions in cognitive profiles in this population. Such distinctions may be important for interpreting research findings and in clinical decisions about how best to assess autistic abilities. We are presently assessing whether similar instrument-specific gender differences are manifested in children and adolescents on the autism spectrum.

144.148 148 Individual Differences in Homograph Reading Amongst Hebrew-Speaking Autistic Children. J. Brock*¹, N. Sukenik² and N. Friedmann², (1)*Macquarie University*, (2)*Tel Aviv University*

Background: One of the most consistently replicated and influential findings in research on autistic cognition is the poor performance of individuals with autism on tests of homograph reading. In the test, participants are required to read aloud sentences containing ambiguous words such as "tear" that are pronounced differently depending on their meaning. According to the weak central coherence account, poor performance reflects a failure of language comprehension: words are processed out of context, hence the appropriate meaning and pronunciation are not extracted. However, this account is not supported by evidence from other paradigms such as semantic priming and language-mediated eye-movements. Furthermore,

significant group differences mask the fact that many participants with autism perform at ceiling on the test.

Objectives: In the current study, we investigated individual differences in homograph reading amongst autistic children who spoke Hebrew as their native language. Hebrew is characterized by a high degree of orthographic ambiguity and provides many more suitable homographs than English. We were therefore able to obtain reliable individual differences and determine predictors of performance within the group of autistic children.

Methods: Participants were 18 native Hebrew-speaking autistic children (16 boys) aged 8;3 to 17;6 years (mean = 11;7, SD = 1;8), rigorously diagnosed by a multi-disciplinary panel. In the homograph reading task, participants read aloud 26 sentences containing homographs whose correct pronunciation depended on the preceding sentence context. In addition, participants completed a battery of language and reading tests and teachers completed the Childhood Autism Rating Scale (CARS) for each child. Data were analysed using logistic regression with mixed random effects.

Results: There was, as expected, considerable variation in performance across participants, with scores ranging from 58 to 96% correct. Significant predictors of accuracy included age, CARS score, word reading (but not nonword reading), and paragraph reading speed and accuracy. However, the best predictor was picture naming. This accounted for unique variation beyond each of the other predictors. Indeed, the logistic regression model containing picture naming left no significant individual variation in homograph reading unaccounted for.

Conclusions: The results confirm that there is considerable and reliable individual variation in homograph reading amongst autistic children. Moreover, they suggest an interesting new explanation for the homograph-reading difficulties. Performance was best predicted by picture naming which, like homograph-reading, involves the selection of one spoken form from amongst multiple possible candidates. Thus, difficulties in homograph reading faced by some autistic individuals may originate in the processes of speech production rather than in

comprehension and the use of sentence context, as the central coherence account assumes. The results highlight the importance of investigating individual differences within the autism spectrum and demonstrate the novel insights this can bring to understanding of autistic cognition.

144.149 149 Inhibition of Eye Blinking Reveals Subjective Perceptions of Stimulus Saliency in Children with Autism Spectrum Disorder. S. Shultz*, A. Klin and W. Jones, *Marcus Autism Center, Children's Healthcare of Atlanta & Emory University School of Medicine*

Background:

Altered engagement with the social world is posited to be both cause and consequence of the social and communicative deficits characteristic of Autism Spectrum Disorders (ASD). By attending to less socially relevant aspects of a scene, individuals with ASD may be missing socially adaptive information, setting them on an altered path for learning. This cycle is then likely to build iteratively over the course of a child's development. While eye-tracking quantifies where individuals look when viewing social scenes, these measures fail to capture how *engaged* a viewer is with what he is attending to. Even knowing what a child with ASD looks at, we are left to wonder what aspects of that scene are perceived as being particularly important or most relevant to process? The answer to this question will shed light on cues that capture the attention of individuals with ASD, and may identify (1) factors that adversely impact the efforts of individuals with ASD to make sense of complex social environments and (2) compensatory learning strategies that have adaptive value for individuals with ASD.

Objectives:

Our aims are to investigate: (1) what types of stimuli are perceived as being highly engaging by children with ASD; and (2) how different patterns of visual engagement are related to an individual's social and cognitive functioning.

Methods:

People spontaneously inhibit blinks when processing salient stimuli in order to minimize the loss of visual information that occurs when

blinking. Exactly when inhibition occurs marks the viewers' subjective assessment of how engaging a stimulus is (Shultz, Klin, & Jones, 2012). Given this, we used blink inhibition to measure between-group differences in engagement and then examined the properties of stimuli that were perceived as highly engaging by children with ASD. Engagement was quantified in children with ASD (n = 49) and typically-developing children (n = 26) as they viewed movie scenes of social interaction.

Results:

As predicted, children with ASD and their typically-developing peers differed significantly in their timing of blink inhibition relative to scene content. Preliminary analyses offer quantitative evidence that children with ASD are engaged by rapid changes in visual content, such as those that follow movie scene cuts. Children with ASD show increased engagement after scene cuts, regardless of the social adaptive value of the new information presented. Ongoing analyses are aimed at examining in greater detail the perceptual properties of stimuli that elicit increased engagement in children with ASD, and then relating varying profiles of engagement to clinical measures of social disability and cognitive functioning.

Conclusions:

The present study furthers our understanding of altered social engagement in ASD by examining not only where a child is looking but how engaged a child is with what he is looking at. The current results point to one factor that may disrupt processing of complex social scenes in children with ASD: changes in visual information elicit high levels of automatic engagement, making it more challenging to seek out other environmental cues that may contextualize the novel information.

144.150 150 Intentional Control and Behavioural Rigidity in Individuals with Autism. E. Poljac*, *Radboud University Nijmegen*

Background: Different clinical studies have provided empirical evidence for impairments in cognitive control in individuals with autism spectrum disorders (ASD). These cognitive control impairments become evident as rigid and

repetitive patterns of behaviour. The challenge arises, however, when trying to specify the neurocognitive mechanisms behind the reported observations of deviant patterns of goal-directed behaviour in ASD. In fact, studies trying to test specific assumptions by applying designs that are based on a more controlled experimental conditions often fail in providing strong evidence for an impairment in specific cognitive functions.

Objectives: The main objective of this study is to test the idea recently put forward in the literature that the preference for repetitive behaviour in ASD reflects intentional deficits rather than problems at the level of the implementation of intentions. We tested the idea of problems with intentional control— a specific subset of cognitive control processes that biases the choice of our behavioural goals—in the broader autism phenotype.

Methods: Participants were healthy individuals with either a low or a high number of autistic traits as measured by a self-report questionnaire that quantifies the extent of autistic traits in healthy population—the Autism-spectrum Quotient (AQ). Participants chose between two tasks differing in their relative strength by indicating first their voluntary task choice and then responding to the subsequently presented stimulus. The tasks included responding to the location or responding to the shape of the presented stimuli. This voluntary task-switching paradigm allowed us to disentangle the intentional task choice from its implementation at the level of task execution (i.e., responding to the presented stimulus).

Results: The findings demonstrate a significantly stronger tendency to repeat tasks more often for the participants with high level of autistic traits. Crucially, while the patterns of task choice showed a stronger bias toward repeating the harder task in participants with more autistic traits, no differences in behavior during actual task execution were found between high and low AQ participants.

Conclusions: The present study indicates that the tendency of individuals with autism to engage in repetitive behavior arises at the level of the formation of task intentions when tasks are chosen voluntarily. Our results reveal that the way

in which global task intentions are formed—as measured by behavioral patterns in task choice—depends on the quantification of where an individual lies along the dimension of autistic traits. On the contrary, the way that tasks are being executed—as measured by behavioral patterns in RTs and errors—seems not to be related to the amount of autistic traits in healthy individuals.

144.151 151 Investigating and Training Gaze Control Using Eye-Tracking and Virtual Humans. J. Nadel^{*1}, J. C. Martin² and O. Grynszpan³, (1)*French Centre of Scientific Research*, (2)*CNRS/ Université paris-Sud*, (3)*Université Pierre & Marie Curie/CNRS*

Background: The use of gaze as a communication channel is considered altered in Autism Spectrum Disorders (ASD). There are currently different bottom-up hypotheses that link the difficulties in communication and social interactions with atypicalities in social gaze. Multimedia interactions based on eye-tracking and virtual reality offer new opportunities for investigating and training gaze behavior in social contexts. In a previous study, we designed a novel system that placed participants face-to-face with a virtual human while providing real time biofeedback on the position of the participant's gaze via eye-tracking technology. In the present study, our system displays short videos of real social interactions to test whether the previous findings remained valid in a context closer to real life settings.

Objectives: The goal of the project presented here is to offer new tools and methods for assessing and training social gaze, based on experimental data and adequate theoretical grounding regarding people with Autism Spectrum Disorder.

Methods: The eye-tracking system that we designed enables simulating a gaze-contingent viewing window: the entire visual display is blurred in real-time, except for a rectangular area centered on the focal point of the participant. Thirteen participants with High Functioning Autism Spectrum Disorders (HFASD) were recruited. They watched two short movie extracts that involved social interactions between three actors. In both extracts, two of the actors were behaving hypocritically towards the third actor, displaying facial expressions and gaze behaviors that

contradicted what they were saying. The video extracts were shown in two different conditions: a control condition allowing free visual exploration and an experimental condition using the viewing window. After each video extract, participants were asked to explain what they had seen. Their responses were coded by two independent judges who counted the number of mentalising verbs (e.g. think, believe, know...).

Results: The average duration of fixations was positively correlated with the ratio of mentalising verbs only when the gaze-contingent viewing window was used. This outcome confirms our previous conclusion (Grynszpan et al., 2012) that the system induces a situation where the visual behavior of participants with HFASD is closely linked to their cognitive understanding of social exchanges.

Conclusions: This link seems highly relevant for training gaze control in relation with the interpretation of social interactions. We are currently constructing and testing an intervention based on our system.

144.152 152 Local and Global Processing and the Effect of Context On Social and Non-Social Processing in High Functioning Adolescents with ASD. D. Ben-Yosef*, D. Anaki and O. Golan, *Bar-Ilan University*

Background:

Cognitive abnormalities in Autism Spectrum Disorders (ASD) have been attributed to a preference for local processing, alongside global processing difficulties. Whereas local processing focuses on the details, global processing aims for a more holistic, integrative picture. An important skill, often associated with global processing, is the ability to use context. Yet, research findings regarding the ability of individuals with ASD to understand context have been inconclusive.

A common paradigm that enables a separate assessment of local and global visual processing uses stimuli that have been filtered to reveal only high or low frequency bands, respectively. Studies that have used this paradigm with social stimuli, described a tendency for local processing among individuals with ASD. However, no such studies examined the high and low frequency processing of non-social stimuli. Furthermore, the ability of

individuals with ASD to use context in order to enhance their global visual processing has not been previously explored.

Objectives: This study examined the ability of high functioning adolescents with ASD to use context when processing social and non-social stimuli, and their ability to harness contextual information in support of their processing of these visual stimuli.

Methods: Sixteen children and adolescents (aged 11-17) with ASD and sixteen Typically Developing (TD) controls, matched on chronological and mental age, took two computerized recognition tasks, one presenting social stimuli (facial expressions) and the other presenting non-social stimuli (animal face photos). In order to examine the ability to use context, each visual stimulus was preceded by an auditory prime that was either congruent, incongruent, or neutral to it. In order to examine local and global processing style in each task, visual stimuli were presented in three spatial frequency conditions: High Frequency (HF), Low Frequency (LF), and Broad-Band (BB). Response time for correct responses was recorded for each condition.

Results: Reaction time analyses for both social and non-social stimuli confirmed main effects of group (TD<ASD), context (Congruent<Incongruent=Neutral), and spatial frequency (BB<LF=HF). Analysis for reaction time to facial expressions showed no group by context interactions on HF and BB spatial frequency conditions. However, on the LF (i.e., global) condition, only the TD group performed faster on the congruent condition, compared to the incongruent and neutral conditions, whereas the ASD group showed no such improvement due to supporting context. Analysis of reaction time to non-social stimuli showed no significant interactions with group.

Conclusions: High Functioning adolescents with ASD show intact global and local visual processing of both social and non-social stimuli. However, their ability to support global processing of social stimuli through the use of context is compromised. These findings may affect our understanding of current cognitive theories of ASD and their clinical applications.

144.153 153 Model-Based Learning and Enhanced Systemising Ability in High Functioning Autism and Asperger's Syndrome. D. J. Fowler*, *University of Sussex*

Background:

Restricted and repetitive interests/behaviours and need for sameness represent an important source of impairment for individuals with autism-spectrum-conditions (ASC) yet their relationship to altered decision-making processes have rarely been investigated. This is surprising given that impaired decision-making processes are central to another neurodevelopmental disorder e.g. impaired delayed discounting in ADHD (Barkley et al., 2001; Ellen Demurie, 2010) .

Here we used a hierarchical decision making task (Daw et al., 2011) to investigate whether individuals with ASC tend to adopt simple model free or alternate more sophisticated model-based strategy that require generation of an internal model of the task structure. We predicted that unlike individuals with other forms of compulsive behaviour e.g. OCD who are predicted to use simple model-free approaches, individuals with ASC who show greater systematising are more likely to use model-based strategies.

Objectives:

Determine whether the use of sophisticated model-based strategies is affected by ASC.

Methods:

11 ASD (7 male, mean age 42 ± 14) and 11 control (3 male, mean age 24 ± 4) participants were recruited. Each performed the task 2 times, each consisting of 67 iterations, following a comprehensive tutorial. AQ, EQ, NART, BDI and STAI questionnaires were also administered to measure mood and IQ.

In the task there were two stages: a transition stage where choices govern the probability of being presented with different pairs of stimuli in the next stage, namely the reward stage which determines the probability of being rewarded. The task was computerised, and controlled using the keyboard. I used standard RL equations to model participants' estimates of reward and transition

probabilities. The model was a hybrid of model-based and model-free RL, the ratio of use between these two sub-models being determined by a parameter.

Results:

Participants with autism showed greater use of model based RL ($T_{(11)}=2.4, p<0.05$) . AQ correlated with use of model based RL ($R^2=0.30, p<0.05$), while IQ did not ($R^2=0.035, p>0.05$). Recruitment is ongoing and full results will be presented at the conference. Effects remained significant after controlling for age.

Conclusions:

Our provisional results suggest an increased tendency to model-based decision-making processes in ASC. This is interesting as it is in contrast to predictions that individuals with other types of repetitive behaviour e.g. OCD or compulsive drug are more likely to use model-free strategies. This insight may help explain why restrictive/repetitive behaviours are resistant to conventional CBT approaches developed for OCD and may help inform refinements of these. Performance on this task may also suggest an alternate way of indexing tendency to systematise in ASC.

144.154 154 No Evidence for Reduced Global and/or Enhanced Local Visual Processing in Adolescents with ASD: Evidence From Embedded Figures and Configural Superiority Tests. C. Dillen*¹, B. Boets², H. P. Op de Beeck³ and J. Steyaert⁴, (1)*Department of Neurosciences, University of Leuven (KU Leuven)*, (2)*University of Leuven (KU Leuven)*, (3)*University of Leuven*, (4)*Maastricht University Hospital*

Background: Atypical sensory processing is often reported in autism spectrum disorders (ASD). Two of the most prominent theories, the Weak Central Coherence (WCC) and the Enhanced Perceptual Functioning (EPF) account, postulate that individuals with ASD are characterized by a weak or absent drive for global coherence and/or a superior processing of local details. A classic example of this local processing bias in ASD is the superior performance on the embedded figures test. The well-known configural superiority task (Pomerantz, Sager & Stoeber, 1977) constitutes a very simple and 'pure' version of this embedded figure test. In this task, subjects have to identify

the oddly oriented item in a display of four items, constituted either by four single lines (part condition) or by the same four lines with identical corners added to it (whole condition). In typically developing individuals there is overwhelming evidence for superior performance on the whole condition as compared to the part condition.

Objectives: In the present study we aimed to determine whether performance on the configural superiority task in high functioning individuals with ASD is less influenced by the context when processing 'parts' versus 'wholes'.

Methods: A sample of 20 high functioning adolescents with ASD and early language delay was recruited (mean age 16 years, range 13-21 years), as well as a sample of 20 typically developing controls, matched for age and performance IQ (mean age 16 years, range 14-20 years). All participants performed a forced-choice computerized version of the embedded figures task and the configural superiority task.

(Preliminary) Results: Controls were significantly faster and more accurate than individuals with ASD on the embedded figures test. On the configural superiority task, both groups presented an advantage of processing wholes versus parts, both in terms of accuracy and in terms of reaction times. Yet, there was no significant group difference or group by condition interaction, implying that both groups were equally influenced by the context effects of processing 'parts' versus 'wholes'.

Conclusions: Adolescents with ASD showed no superior performance on the embedded figures task. Quite the contrary, they even performed significantly more poorly. Both groups were also equally sensitive to the context when processing 'parts' versus 'wholes' in the configural superiority task. Taken together, these findings do not support the hypothesis of reduced global or enhanced local visual processing as postulated by the WCC or EPF theories.

144.155 155 Object-Location Memory in Autism Spectrum Disorder.
M. Ring*, D. M. Bowler and S. B. Gaigg, *City University London*

Background: Evidence suggests that individuals with Autism Spectrum Disorder (ASD) show

problems with binding together parts of an event (Bowler et al., 2011; in *Researching the autism spectrum: Contemporary perspectives*, 316-346). Other evidence suggests that these individuals tend to have intact implicit memory but subtle difficulties with explicit memory for verbal material (Gardiner et al., 2003; *JADD*, 33, 259-269). When tested for object recognition ASD individuals perform mainly as well as typically developing (TD) individuals (Hauck et al., 1998; *Child Neuropsychol*, 4, 187-198).

Objectives: The aim was to expand existing knowledge to determine if difficulties in explicit memory extend to spatial relational information whilst implicit memory for this information remains intact.

Methods: Sixteen participants with a confirmed clinical diagnosis of ASD and 16 age, gender and IQ matched TD individuals were tested. An object-location memory test was implemented using the process dissociation procedure developed by Jacoby (Jacoby, 1991; *J Mem Lang*, 30, 513-541) to test for explicit and implicit memory. In this task participants studied locations of objects in pictures of rooms presented on a computer screen. In the testing phase participants were shown an object and had to either choose its old location from a choice of three ('inclusion trials') or choose a new location ('exclusion trials'). Eye-movements were also recorded during the test and following the primary 'inclusion/exclusion' test, recognition memory was tested for objects and locations separately using the 'remember-know' procedure.

Results: On inclusion trials ASD individuals chose the old location significantly less often ($F(1,30) = 5.71, p < .05$) but they did as well as the TD individuals on exclusion trials. This led to a significantly lower estimate of explicit memory for the ASD group ($F(1,30) = 5.65, p < .05$) but implicit memory was preserved. This is unlikely to be due to differences between groups in attending to the various response options during the test because both groups looked significantly longer at the old object location during inclusion trials ($F(1,29) = 105.37, p < .001$) and longer at another location during exclusion trials ($F(1,29) = 105.37, p < .001$). The object and location recognition tests indicated that the lower performance of the ASD group in explicit object-

location memory was unlikely to be the result of poorer memory for the objects or locations separately.

Conclusions: This experiment extends findings of diminished explicit memory in ASD from the verbal to the spatial domain and indicates that these difficulties might not be due to differential attention or lower memory for items or locations but rather due to the relation between both. It gives further support for the theory that individuals with ASD seem to have a problem with relational binding and the hippocampus rather than other regions in the medial temporal lobes of the brain.

144.156 156 Relations Among Speed of Attention Shifting, Background Noise, and Symptom Severity in Children with Autism Spectrum Disorders. L. E. Bahrnick and J. T. Todd*, *Florida International University*

Background: Children with autism spectrum disorders (ASD) show impaired attention and intersensory processing skills compared with typically developing (TD) children (Bebko et al., 2006; Bahrnick & Todd, 2012). They show difficulty disengaging attention (Landry & Bryson, 2004; Todd & Bahrnick, 2010) and integrating audiovisual speech in the presence of background noise (Smith & Bennetto, 2007). Findings suggest impairments in ASD are enhanced in the context of competing auditory or visual stimulation.

Objectives: We investigated whether competing background noise would degrade speed of attention shifting in children with ASD to a greater extent than for TDs. Disengagement (shifting away from competing stimulation to a peripheral event) and orienting (shifting in the absence of competing stimulation) were assessed using the Multisensory Attention Assessment Protocol (MAAP; Bahrnick et al., 2011). We predicted that, compared to TDs, children with ASD would show greater impairments in disengagement and orienting when background noise was present vs. absent. We also predicted that greater impairments in attention shifting would correlate with higher symptom severity in ASD.

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 adjusted age (ASD: $M=2.47$, $SD=1.37$; TD: $M=2.77$, $SD=.77$) 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, were presented. Peripheral events consisted of social (two woman speaking) and nonsocial events (two objects striking a surface) and were presented with and without background noise. Disengagement (RT to shift to a peripheral event while the competing central event was on) and orienting (RT to shift to a peripheral event after the central event went off) were assessed. ADOS Standard Scores indexed symptom severity (see Gotham et al., 2009).

Results: Children with ASD showed longer RTs on noise than no noise trials ($p<.03$), whereas RTs for TDs did not differ as a function of noise. ASDs showed longer RTs to disengage and orient than TDs ($ps<.01$); however, this pattern was more extreme during noise trials. On noise trials, ASDs showed longer RTs for both disengaging and orienting than TDs ($ps<.02$). In contrast, on no-noise trials, ASDs showed longer RTs to disengage ($p=.01$) than TDs, but RTs to orient did not differ from TDs. Finally, longer RTs to disengage and orient on noise (but not no noise) trials predicted higher ADOS Standard Scores ($rs>.54$, $ps<.01$) in ASDs.

Conclusions: Children with ASD show significant decreases in speed of disengaging and orienting attention to social and nonsocial events in the presence of noise. Moreover, noise enhances impairments in ASD relative to TD children, but has little effect on speed of attention shifting in TD children. Further, greater impairments in shifting attention are correlated with higher symptom severity in ASD. Findings extend research indicating impaired attention skills in ASD (Landry & Bryson, 2004; Todd & Bahrnick, 2010) and suggest that these impairments will be most evident under conditions of competing stimulation from background noise.

144.157 157 Response Shifting and Inhibition in Preschoolers with Autism Spectrum Disorder. J. Mussey*¹ and L. G. Klinger², (1)*University of Alabama*, (2)*University of North Carolina*

Background: Executive functions (EF) encompass a variety of skills including those that begin to develop early (working memory and inhibition) and those that begin to develop later in childhood (planning and self-monitoring). Previous studies

with children and adolescents found that individuals with autism spectrum disorder (ASD) show impairment on EF tasks requiring mental flexibility and intact performance on tasks requiring inhibitory control (Ozonoff, South & Provençal, 2007). Few studies have examined EF in preschool-aged children with ASD and these studies have largely failed to demonstrate specific EF deficits (Griffith et al., 1999; Dawson et al., 2002). Further, EF deficits in older individuals with ASD have been linked to developmental delay suggesting that EF may be a result of cognitive impairments rather than an autism-specific symptom.

Objectives: The purpose of this study was to examine inhibitory EF in preschool children with ASD. Particularly of interest was the potential relation between other cognitive skills and EF early in development. Thus, links between EF and standardized developmental measures and measures of imitation were examined.

Methods: Participants included 25 young children with ASD (chronological age: mean = 43 months; range 25-68 months) and two groups of children with typical development (29 matched on chronological age, mean = 43 months; 28 matched on receptive language ability, mean = 37 months). The Mullen Scales of Early Learning was administered to measure nonverbal abilities as well as receptive and expressive language. Children completed an assessment of imitation, the Motor Imitation Scale (MIS; Stone et al., 1997) and two EF measures of inhibition, A-not-B Task and Gift Wrap Delay.

Results: EF was measured by overall performance and error rates. Compared to chronological-aged matched children with typical development, children with ASD showed similar levels of EF, all $t(52) < 1.66$, all p 's $> .10$. Compared to receptive language ability matched children with typical development, children with ASD showed similar levels of EF, all $t(51) < 1.28$, all p 's $> .20$. For children with ASD, correct choices on the A-not-B Task were significantly positively correlated with standard scores on nonverbal development and language (r 's $> .43$, p 's $< .032$) and measures of imitation (r 's $> .40$, p 's $< .047$). On the Gift Delay task for children with ASD, number of times peeked while waiting was significantly negatively correlated with expressive language and overall

Early Learning Composite (r 's $< -.41$, p 's $< .041$). Data for both groups of children with typical development were combined for correlation analyses. For all children with typical development no significant correlations were found between any EF measure, imitation, nonverbal or verbal abilities.

Conclusions: Results support the notion that inhibitory EF is not impaired in preschool-aged children with ASD. No relation between EF and developmental level was found in children with typical development, whereas for children with ASD better performance on EF was related to overall cognitive ability (expressive language and visual reception skills) and imitation ability. The causal relation between early developmental delays and later EF impairments is largely unknown. However, for children with ASD, language development and overall cognitive development could have important implications for the later development of EF ability.

144.158 158 Semantic Memory Structure in Children and Adolescents with Autism Spectrum Disorder. K. M. Rancourt^{*1}, J. H. Filliter¹, P. A. McMullen¹ and S. A. Johnson², (1)*Dalhousie University*, (2)*IWK Health Centre*

Background: Learning and memory abilities are fundamental to the application and generalization of skills acquired in Autism Spectrum Disorder (ASD) treatment programs. One important aspect of learning and memory is semantic categorization, whereby related concepts are grouped and linked to form an organized semantic memory system. Categorization processes occur hierarchically across three different levels: superordinate ('Animal'), basic ('Dog'), and subordinate ('Beagle'; Rosch & Lloyd, 1978). Typically developing individuals (TD) identify objects fastest at the basic level (Jolicoeur et al., 1984), indicating it as the usual entry point into semantic memory. In addition, TD categorize living objects with different proficiency than non-living objects (McMullen & Purdy, 2006). ASD children appear to categorize according to concrete rather than abstract features (Shulman et al., 1995), and have trouble forming category prototypes (Klinger & Dawson, 2001). The Weak Central Coherence (WCC) theory, which postulates a bias to process detail, may help to explain categorization differences in ASD.

Objectives: 1) To determine if and how categorization differs in ASD compared to TD youths. Based on WCC theory, we expected ASD participants, relative to controls, to demonstrate faster subordinate responses (i.e., most specific) and slower superordinate responses (i.e., most general). 2) To examine relationships between categorization and central coherence performance.

Methods: To date, our sample includes 19 high-functioning youths (aged 8 to 18 years) with ASD and 16 age-, sex-, and IQ-matched TD participants. Participants were shown word and line drawing pairs of living (dogs, bugs, birds) and non-living (cars, boats, aircrafts) objects to match at the three levels of categorization. The Embedded Figures Test (EFT) was employed as a measure of central coherence.

Results: A Level (basic, subordinate, superordinate) x Group (TD, ASD) mixed Analysis of Variance of correct response times to match trials, revealed an effect of Level, $F(2,64) = 13.48$, $p < 0.001$, only. For the ASD, better performance on the EFT (i.e., weaker central coherence) was related to slower responses at basic ($r(19) = -0.53$, $p < 0.05$) and superordinate ($r(19) = -0.65$, $p < 0.01$) levels. EFT performance was not correlated with responses at any level for the TD. Separate analyses of responses to living and non-living objects provided preliminary support for our hypothesis with living objects: ASD categorized slower at the superordinate level ($d = 0.24$) and faster at the subordinate level ($d = 0.29$) than the TD. ASD categorized non-living objects slower than the TD at both basic ($d = 0.28$) and subordinate levels ($d = 0.24$).

Conclusions: Consistent with WCC theory, results provide preliminary evidence that youths with ASD categorize living objects slower than their TD peers at the superordinate (most general) level and faster at the subordinate (most specific) level. Weaker central coherence was associated with slower categorization at more general levels. In contrast, ASD participants categorized non-living objects slower than TD youths at the subordinate and basic levels. Results indicate that semantic memory organization and processing differs between ASD and TD youths and that the living/non-living distinction is an important direction for future studies.

144.159 159 The Factor Structure of the Behavior Rating Inventory of Executive Function in Children and Adolescents with Autism Spectrum Disorders Replicates the Normative Sample. Y. Granader*¹, B. E. Yerys², G. L. Wallace³, R. Lawson¹, M. Rosenthal⁴, M. Wills¹, E. Dixon⁵, L. G. Anthony¹, J. Pandey², R. Thompson², R. T. Schultz² and L. Kenworthy¹, (1)Children's National Medical Center, (2)Children's Hospital of Philadelphia, (3)National Institute of Mental Health, (4)Child Mind Institute, (5)National Institutes of Health

Background: Children with autism spectrum disorders (ASDs) have a high rate of executive functioning deficits, which can cause great difficulty in daily activities at both school and home. Given that executive function weaknesses are more common in children with ASDs than in the general population, it is important to screen for executive dysfunction in order to recommend appropriate clinical interventions. The Behavior Rating Inventory of Executive Function (BRIEF) assesses executive functioning skills in daily life. The psychometric properties and clinical utility of the BRIEF have been examined in clinical populations. Elevated BRIEF scores have been reported in ASD; however, the factor structure of the BRIEF has not been explored in this population.

Objectives: To investigate the factor structure of the BRIEF in a large sample of children with ASDs and to determine the frequency of BRIEF scale elevations in this sample.

Methods: 479 children with ASDs (405 males and 74 females, age range 5-18 years, mean = 10.6, SD = 3.2) were assessed at Children's National Medical Center, National Institute of Mental Health, and the Children's Hospital of Philadelphia. Participants with an IQ below 70 were excluded from this study. IQ ranged from 70-158 (mean = 101.0, SD = 17.7). Parents completed the BRIEF as part of a research protocol or neuropsychological evaluation. BRIEF scale elevations were determined to be of "potential clinical significance" (Gioia et al., 2000, p. 14) if the T-score was at or above 65. Principal component analyses (PCA) with oblique (promax) rotations were performed on the BRIEF subscale T-scores in order to explore the underlying structure.

Results: Subscale elevations were generally consistent with previous research in ASD. The Shift, Initiate, Working Memory, Plan/Organize, and Monitor subscales were elevated in 51 to 63% of the sample. The PCA revealed one factor that accounted for 57.1% of the variance. When a two-factor solution was forced factor loadings ranged from .54 to .97. Five of the scales loaded highly on the first component (Plan/Organize, Working Memory, Organization of Materials, Initiate, and Monitor) and three of the scales loaded predominantly on the second component (Emotional Control, Shift, and Inhibit). No cross factor loadings were found. The two constructs defined by these component loadings replicated the original normative data in the BRIEF manual identifying two indices: Behavioral Regulation and Metacognition.

Conclusions: This study provides preliminary psychometric and clinical descriptive data about the BRIEF subscale scores in a large sample of children with ASDs. The results of this study are similar to previous findings, which indicate that a substantial proportion of children with ASDs display significant difficulties with executive functions as measured by the BRIEF subscales. In addition, the PCA revealed one factor that corresponded to the original Global Executive Composite and when a two-factor solution was forced the factor structure corresponded to the original Behavioral Regulation and Metacognition Indices, and provided validation for using normative BRIEF data with children with ASDs. Future studies should use confirmatory factor analysis in order to further examine the validity of the BRIEF with this population.

144.160 160 The Influence of Emotional Valence On Prospective Memory Performance in Children with High-Functioning Autism Spectrum Disorders. A. Kretschmer* and M. Altgassen, *Technische Universitaet Dresden*

Background: Prospective memory, the ability to remember intentions at a certain point in the future, is important for performing everyday tasks and to cope with daily demands. Prospective memory deficits in autism spectrum disorders (ASD) have been related to executive dysfunctions (e.g., Altgassen et al., 2009, 2012). Until now, no study has explicitly tested the impact of executive control load on prospective memory performance in ASD. Emotionally salient prospective memory cues are assumed to reduce executive control

demands compared to emotionally neutral cues and to improve prospective memory performance by reducing the need for monitoring and facilitating switching from the ongoing task to the intended action (cf. studies in older adults, e.g., Altgassen et al., 2010).

Objectives: The present study aimed at investigating the influence of emotional valence of prospective cues on prospective memory performance in children with ASD for the first time.

Methods: Eighteen children with high-functioning ASD and 18 typically developing individuals parallel for age, verbal and non-verbal mental abilities participated in this study. A laboratory-based task was used to investigate prospective memory performance. For the ongoing activity, a 2-back working memory task was used. Colored pictures were presented and participants were asked to indicate by keypress if the presented picture was the same as the picture presented two pictures before or not. Six prospective memory stimuli were presented (2 positive, 2 negative and 2 neutral stimuli) and participants were instructed to remember to press a third key if one of the prospective memory cues was presented. After a filled delay, the dual task block consisting of the ongoing task and the prospective memory task, started.

Results: An analysis of variance with repeated measures revealed a significant main effect of emotional valence of prospective memory stimuli. Overall, more emotionally negative stimuli were remembered correctly than emotionally positive and neutral stimuli. The group effect was also significant, indicating that children with ASD had less prospective memory hits than typically developing controls. Further analyses revealed that children with ASD had more prospective memory hits when emotionally positive and negative prospective memory stimuli were presented as compared to neutral ones. Controls had more prospective memory hits to emotionally negative stimuli than to positive and neutral ones, while prospective memory performance did not differ between emotionally positive and neutral prospective memory cues.

Conclusions: Overall, controls outperformed individuals with ASD in a standard laboratory

prospective memory task. Both groups benefited from the emotional valence of prospective memory stimuli. Specifically, individuals of the ASD group benefited from emotionally positive and negative prospective memory cues, while controls' prospective memory performance only increased with emotionally negative cues. Results indicate that emotionally salient prospective memory cues reduce executive control load on prospective memory tasks. Future studies should examine if everyday prospective memory performance in ASD can be enhanced by introducing prospective memory tasks in an emotional salient way.

144.161 161 Transitive Inference Learning in Children and Adolescents with ASD. J. S. Beck*¹, P. C. Mundy², W. Jarrold³, K. Kim⁴, M. Gwaltney⁵, N. McIntyre⁶, S. Novotny⁷, L. Swain⁷, T. Oswald⁷ and M. Solomon⁸, (1)UC Davis MIND Institute, (2)University of California at Davis, (3)UC Davis, (4)MIND Institute, UC Davis, (5)University of California Davis, Learning & Mind Sciences, (6)U.C. Davis, (7)University of California, Davis, (8)University of California, Davis M.I.N.D. Institute

Background : Individuals with ASD exhibit impairments in generalizing (transferring) learning to new situations. Transitive inference – learning a series of ordered stimulus pairs (AB, BC, CD, EF where A>B>C>D>E), and then transferring this learning about order to novel pairs (AC, AD, AE, BD, BE, CE) -- is a form of generalization. Previously, we examined TI in young adults with ASD and TYP (Solomon, Frank, Smith, Ly, & Carter, 2011), and found that ASD used a strategy involving rote memorization, whereas TYP employed a more flexible strategy using information about the reinforcement value of the hierarchy end-items. Due to the use of a rote memory strategy, the ASD group performed comparably to TYP on the harder BD pair, but worse on the easier AE pair—essentially “missing the forest for the trees” in grasping that A is always right while E never is.

Objectives : We extend the investigation of this pattern of findings to children and adolescents by examining their strategy use; its cognitive correlates; and its relationship to school achievement and age. Given that problems with generalizing learning negatively impact the academic performance of those with ASD, this investigation holds the potential to inform the

development of important and widely-implemented remediation strategies.

Methods : Participants included 23 high functioning children and adolescents ages 8-16 with ASD, qualified using community diagnosis plus ASSQ, SCQ, and DSM-IV criteria, and 23 age, IQ, and gender matched children with TYP. They completed a TI task previously used in TYP children (Townsend, Richmond, Vogel-Farley, & Thomas, 2010), which included training on four stimulus pairs of colored ovals, with subsequent testing on novel pairs. WASI and WIAT-II, were used to assess cognitive abilities and academic performance.

Results : Replicating prior results, during training, a 2x2 ANOVA demonstrated the ASD group used more of a rote memory strategy as evidenced by a significant group by pair type interaction, with the ASD group performing worse on outer pairs ($F(1, 43) = 4.85, p = .043$). At test, the ASD group showed intact performance on the BD inference pair, but significantly worse performance on the BE ($t(48) = 2.29, p = .03$), CE ($t(43) = 2.82, p = .03$), and AE pair at a trend ($t(43) = 1.9, p = .06$). For both groups, using a reinforcement learning strategy was positively associated with Verbal IQ and age, while using a rote memory strategy, was associated with only Performance IQ. In both groups, training trial accuracy was positively related to Math Problem Solving ($r = .529, p = .001$).

Conclusions: Most of the high functioning children with ASD in this study used a TI problem solving strategy that was sub-optimal and relied more on visuo-spatial versus verbal information. Furthermore, performance relying on this strategy did improve with age. TI strategy may be an important individual difference variable to consider when teaching math and other subjects to children and adolescents with ASD, most of whom employ a visuo-spatial, versus a verbal problem solving approach, relative to TYP.

144.162 162 Understanding Time Estimation in Autism Spectrum Disorders. J. A. Burack*¹, C. Gordon Green¹, H. Flores¹, J. L. Ringo² and D. Brodeur³, (1)McGill University, (2)McGill University, (3)Acadia University

Background: Evidence that persons with autism spectrum disorders (ASD) are less able to

accurately estimate temporal durations is interpreted as indicating a widespread deficit in time perception (Allman et al. 2011; Maister & Plaisted-Grant, 2011; Martin et al. 2010). However, this evidence is only from tasks involving longer durations (>1000ms). Conversely, in an initial study with shorter durations, Mostofsky et al. (2000) found no estimation difficulties among high-functioning individuals with ASD. In order to extend Mostofsky et al.'s findings, we studied time perception of a short duration among low-functioning children with ASD in relation to mental-age (MA) matched children and adolescents (youths) with Down syndrome (DS) and typically developing (TD) children.

Objectives: We extended the study of temporal perception among persons with ASD by examining the estimation of short durations in functioning children with ASD as compared to that of MA-matched youths with DS and TD children.

Methods: Currently, the groups (ASD, DS, TD) are each comprised of 10 participants and are matched on an approximate MA of 6 years. Group matching was based on scores from the Leiter-R International Performance Scale Revised (Leiter-R; Roid & Miller, 1997) with p-values for group differences greater than 0.10 for all comparisons. The groups differed in mean age (DS = 15 years; ASD = 10 years; TD = 6 years). All participants completed a temporal bisection task using auditory stimuli. Standard durations of 200 and 800 ms were compared to a range of comparison durations from 200 to 800 ms. After familiarization with the standard durations, participants were asked if each comparison tone was more like the short or the long tone over a series of trials. The primary dependent variable was the proportion of long responses made for each comparison duration condition.

Results: Preliminary analyses yielded a significant Group by Duration interaction, reflecting different patterns of responding across the groups. Participants with ASD reported more "long" responses at the shorter durations and fewer "long" responses at the longer durations than the other groups. The patterns of the DS and TD groups were similar, although youths with DS produced slightly fewer long responses in the longer duration condition. The shallow slopes of

the functions produced by the children with ASD indicate a lack of sensitivity to duration differences. Psychophysical measures of sensitivity have been acquired (e.g., Weber fractions).

Conclusions: Contrary to Mostofsky et al.'s (2000) findings with high functioning persons with ASD, we found poorer sensitivity to the variability of durations under 1000ms among a group of low-functioning children with ASD. The ASD group, with an average MA of 5.9 years, produced bisection functions that suggest poorer sensitivity to time at these durations than was reported for TD children at 5 years of age (McCormack et al., 1999). However, the DS and TD groups produced functions consistent with their developmental level. This is preliminary evidence of an ASD specific deficit in time estimation.

144.163 163 Visual Memory Profile in Children with Autism: The Role of Cognitive Flexibility. S. Semino*, M. Zanobini and S. Solari, *University of Genoa*

Background:

According to several studies, people with High Functioning Autism (HFA) show preserved abilities in recognition memory (e.g. Boucher, Bigham, Mayes & Muskett, 2008) and cued recall (e.g. Mottron, Morasse & Belleville, 2001), and impaired abilities in memory for emotion-related or person-related materials (e.g. Lind, 2010). Results are mixed in working memory and source memory (e.g. Bigham, Boucher, Mayes & Anns, 2010). On the other side, most of the limited number of research projects involving people with Low Functioning Autism (LFA) highlight inconsistent findings and a less defined pattern of memory functioning.

Objectives:

- to evaluate different areas of visual memory abilities in children with LFA and HFA
- to explore the relationship between memory, cognitive functioning and cognitive flexibility
- to compare the memory profile of children with LFA and HFA.

Methods:

The pilot sample is composed of 6 children with LFA (mean age = 10.4) and 6 children with HFA (mean age = 10). Evaluation are still ongoing for a second group of children.

Brief IQ of Leiter-R was used to evaluate cognitive functioning. Memory profile was evaluated using the following tasks:

- Memory for Faces (TEMA, Test di Memoria e Apprendimento – TOMAL),
- Corsi Tapping Test,
- Associated Pairs, Forward Memory, Immediate Recognition, Delayed Recognition and Delayed Pairs (Leiter-R).

The Dimensional Change Card Sort Test (DCCS) was used to assess cognitive flexibility.

Results:

Memory profile

The Wilcoxon test was used to compare both subtest results and composite scores. In the group with LFA we found that Sequential Order is lower than Form Completion (p .042), and that Associative Memory composite score is higher than Fluid Reasoning (p .043), IQ Brief (p .043) and Recognition Memory (p .042). Furthermore we found that Associated Pairs is higher than Forward Memory (p .042) and Memory for Faces (p .041).

The Mann-Whitney test highlighted similar memory performance in children with HFA and LFA, except than in Memory for Faces where HFA group perform better than LFA group (p .004).

Cognitive Flexibility (DCCS)

None of the children with LFA was able to pass the third phase and the number of total correct answers given by LFA is lower than that given by HFA (p .049). In children with HFA the number of total correct answers given in phase three, correlates with several memory measure. We split the sample in two groups depending on the

passing of phase three and we found that the two group show significant difference in several aspects of memory and cognitive functioning.

Conclusions:

Our results suggest that children with autism may have quite intact ability in the associative memory, while they can experience various difficulties in sequential thinking, sequential memory, generation of rules and abstraction.

Flexibility is confirmed to be a weakness in the cognitive profile of autistic children and seems to have a role also in visual perceptive task and in associative memory task, influencing both weakness and strengthens in the performance.

144.164 164 Visual Search and Attention in Children with Autism Spectrum Disorders--- an Eye-Tracking Study. C. Wang*, Z. Wang, S. Gao, S. Jin, Q. Li and H. Zheng, *Nankai University*

Background:

Abnormalities of visual attention or perception have been reported to appear inherent in a number of behaviors observed in ASD. Individuals with ASD often show enhanced performance relative to non-ASD individuals, for example, individuals with ASD have been found to excel in the Embedded Figures Task (Joliffe & Baron-Cohen, 1997; Shah & Frith, 1983) and visual search (Kemner, van Ewijk, van Engeland & Hooge, 2008; O’Riordan & Plaisted, 2001; Joseph, Keehn, Connolly, Wolfe & Horowitz, 2009), but there has been relatively little attention paid to their cognitive mechanism and memory.

Objectives:

The objective of the study is to examine the contributions of both memory and enhanced perceptual processing to visual search and attention in children with ASD and typically developed (TD) children when they are identifying neutral faces.

Methods:

Participants attended two tests. **Short-term memory test:** In this test, 18 children with ASD and 22 age matched TD children were asked to

watch 5 target pictures (5 neutral expression of 5 main characters) and 14 distractor pictures (14 strangers' neutral expression). 5 target pictures successively appeared three times, and 14 distractor pictures appeared only once, so there would be 29 pictures displaying in total. The playback order of pictures would be random. Participants' responses on these pictures were recorded by Tobii TX300. **Long-term memory test:** One week later after the short-term memory test, the two groups were tested again in the same way.

Results:

The results showed significant differences between ASD and TD groups on the fixation duration in the area of interest (AOI) on faces of characters. It was found that ASD and TD children have significant differences on face memory. There are also significant differences in AOIs in short-term memory test between the two groups. It was also found that children with ASD showed superior visual search skills than TD children.

Conclusions:

In summary, ASD search superiority may from anomalously enhanced perception of stimulus features, which was also associated with autism symptom severity.

144.165 165 Working Memory and Visuo-Spatial Cognitions in Toddlers with Autism and Williams Syndrome. G. A. Perminova*, J. A. Burdukova and T. A. Stroganova, *Moscow State University of Psychology and Education (MSUPE)*

Working Memory and Visuo-Spatial Cognitions in Toddlers with Autism and Williams Syndrome

Background: Williams syndrome (WS) is a rare genetic disorder which results in the uneven cognitive profile and unlike an autistic syndrome (AS) is characterized by good social skills. Despite this syndrome specific profile both syndromes are characterized by impairments in working memory and visuo-spatial cognition. We hypothesized that both syndromes would have impairments in working memory and visuo-spatial cognition at early age, caused by the same reason, but

toddlers with WS would have difference in profile of impairments.

Objectives: We examined working memory and visuo-spatial cognition in toddlers with AS and WS in comparison to typically developing children (TDC).

Methods: A-not-B test (Diamond, 1990) was administered to 12 children diagnosed with AS (chronological age ($3,6\pm 0,6$)), 9 children with WS ($3,6\pm 1,2$), and 17 TDC ($2,1\pm 0,7$). Mental age was assessed with Bayley Scales (BSID II, 1993) and Psychological Educational Profile (Schopler et al, 1990). Three groups were matched for mental age. Repeated measures ANOVA was used for statistical analysis.

Results: The results showed that in average the delay in working memory in autistic children was in accordance with their mental age. The WS children showed worse ability to tolerate the delay in AB than both typically developing (TD) and autistic children (AS) matched on mental age. In sharp contrast to both AS and TD groups WS toddlers had problems with maintenance of spatial location of hidden object in their short-term spatial memory. Toddlers with WS had asymmetrical pattern of performance on A-not-B test with the right-handed search errors in simple trials not seen in both AS and TD groups.

Conclusions: Unlike autistic children, toddlers with WS demonstrated a pervasive executive deficit. In addition to worse ability to tolerate the delay in AB toddlers with WS demonstrated left hemisphere deficit in visuo-spatial performance that is not observed in both AS and TD mental age matched groups. This may confirm the hypotheses of left hemisphere impairment in early age Williams syndrome.

144.166 166 Executive Functioning of Children with ASD: An Analysis of the Brief-Questionnaire. M. L. Bezemer* and E. M. Blijd-Hoogewys, *Lentis*

Background:

Children with Autism Spectrum Disorders (ASD) often have problems with Executive Functions (EF). Administering EF tests take a considerable amount of time. A quick alternative can take the form of screening.

The BRIEF questionnaire (Behavior Rating Inventory of Executive Functions; Gioia et al., 2000) screens for EF problems in 5- to 18-year-olds. This questionnaire focuses on potential problems in the areas of inhibition, shifting, emotional control, initiation, working memory, planning and organizing, organization of materials, and monitoring.

Objectives:

The main question is whether there is a specific BRIEF score profile found in children with ASD. The consequential question is whether this profile differs for the three ASD subgroups (Autistic disorder, Asperger's disorder & PDD-NOS). The final question regards the relation between IQ and BRIEF scores.

Methods:

The sample consisted of 127 children between 5 and 18 years old (98 boys, 29 girls). All were diagnosed with a specific ASD (N=35 AD, N=27 AS & N=65 PDD-NOS). Parents filled in a BRIEF questionnaire. All children received an IQ test, the WISC-III.

Results:

The total ASD group (N=127) has significant higher scores - indicative of more EF problems - than the BRIEF norm group on all clinical scales (T-score: $M \geq 50$, $p < .001$), except for Organization of Materials. The shift scale even shows a significant clinical elevation (T-score: $M \geq 65$, $p = .007$).

Each ASD subgroup (AD, AS and PDD-NOS) has the same score profile as mentioned above (T-score: $M \geq 50$, $p = .05-.001$). Regression analysis demonstrates that they do not differ significantly. Next to that, decision tree analysis and hierarchical cluster analysis show that none of the BRIEF variables serve as a predictor for any of the ASD subgroups.

PIQ has significant negative correlations with the BRIEF scales Inhibit, Shift, Working Memory, Plan/Organize and Monitor. However, this is only true if there are no EF problems, except in the case of Inhibit. Also, the greater the distance

between PIQ and VIQ (favoring PIQ), the less EF problems occur.

The negativity scale of the BRIEF - which should serve as a reliability index - deviates in the greater part of the participants (65%). This seems to be due to the fact that most of these items focus on rigidity, which is a main characteristic in ASD.

Conclusions:

The BRIEF is a fairly new instrument. Consistent with other studies, children with ASD show problems on all BRIEF clinical scales, except for Organization of Materials. They have the most profound deficits in cognitive flexibility. No differentiation could be made between the three ASD subgroups, which is in agreement with the DSM-5 proposed revisions: dictating a single diagnostic category.

Based on the results, two recommendations can be made. First, one should take PIQ into account only when interpreting inhibition problems. Overall, the magnitude of the difference between PIQ and VIQ can be of importance. Second, it is advised to omit the negativity scale of the BRIEF as an indication of a negative answer tendency of parents of children with ASD.

144.167 167 Seeing and Saying in Different Language Phenotypes.
C. Norbury*, *Royal Holloway, University of London*

Background: There is great variation within the autism spectrum with regard to viewing social scenes and in providing narrative accounts of depicted events. No previous research has attempted to link how individuals with autism spectrum disorders (ASD) view the social world and how they talk about it. We predicted that both eye-movements and verbal output may be influenced by different neurocognitive phenotypes within ASD.

Objectives: We aimed to answer these key questions: How are the eye-movement patterns of individuals with ASD influenced by (a) the language status of those individuals and (b) social and visual properties of the scenes. Are differences in eye-movement patterns associated with differences in verbal descriptions?

Methods: In two experiments we recorded eye-movements on a Tobii-T120 eye-tracker while participants described simple cartoon events involving two characters. Participants included with autism and language impairments (ALI: n = 14 and 13); autism and language scores within normal range (ALN: n = 15 and 19) and typically developing age-matched peers (TD: n = 17 and 23). Verbal descriptions were transcribed and coded off-line, only accurate, active sentences were included in the eye-movement analysis (e.g. 'the man is feeding the baby'). In Experiment 1, the event occurred in isolation, against a white background. In Experiment 2, the event was situated in a more complex, but contextually appropriate scene. In half of the images, the objects of highest visual salience were the scene characters, and therefore the most socially relevant. In the remaining images, the objects of highest visual salience were in the background and were not central to understanding the depicted event.

Results: In Experiment 1, there were no significant group differences in either fixation sequences or accuracy of verbal responses. In Experiment 2, significant differences emerged in both fixation sequences and verbal responses. The ALI group exhibited significantly different fixation sequences relative to both ALN and TD peers. Similarly, the verbal descriptions of the ALI group were less accurate, reflecting more non-canonical utterances, more dysfluent utterances and more references to irrelevant scene information. However, there was a significant interaction of group and image salience such that these differences were most pronounced when the socially relevant objects were not visually salient. When social and visual salience were overlapping, group differences were attenuated. The ALN group did not differ from TD peers on any measure.

Conclusions: Our visual world is often cluttered and deciding which aspects of a visual scene are the most relevant for attention and comment is crucial for both learning and for pragmatic development. Children with ALI appear to be more prone to distraction, especially when visually salient objects are present. These distractions adversely affect language production, resulting in more laboured and less relevant output. These findings highlight the intimate relationship between language competence and executive

control and point to a therapeutic need to help children with autism and language impairments identify and attend to relevant aspects of their environment.

144.168 168 Adolescents with Autism Spectrum Disorder Do Not Jump to Conclusions. M. Brosnan*, E. Chapman and C. Ashwin, *University of Bath*

Background: People with autism spectrum disorders (ASD) can have difficulties in decision making, often showing indecisiveness and taking longer to make decisions. Individuals with psychosis often make hasty decisions based on little information, which is known as a jumping to conclusions (JTC) reasoning bias. JTC has commonly been shown using the beads task, where people draw beads one at a time from two jars containing different ratios of coloured beads and have to make a decision about which jar they think the beads are being drawn from. The Autism-Psychosis model proposes these disorders represent opposing cognitive profiles, suggesting people with ASD should show the opposite decision making bias to that seen in psychosis.

Objectives: To identify if those with ASD require more information before making a decision than matched controls and to see if this relates to degree of autism symptoms.

Methods: The present study assessed jumping to conclusions in a sample of 23 adolescents with Autism Spectrum Disorder and 20 age-matched controls using the beads task. Short assessments of social and non-social processing were also undertaken. IQ was indexed using the WASI.

Results: Even though both groups showed equivalent levels of confidence in decision-making, the ASD group required more beads than controls before making their decision. Furthermore, a positive correlation was found between increasing information requirements and a greater degree of non-social autism symptoms. No relationship was found with social autism symptoms or IQ.

Conclusions: This is the first study to use the beads task from psychosis research with an ASD sample. The results show a more circumspect decision making bias in ASD, suggesting a more analytic cognitive style when making decisions.

This is the opposite bias to that seen in psychosis, which is consistent with the Autism-Psychosis model.

144.169 169 Lack of Embodied Effects On Stimulus Encoding in High-Functioning Autism. I. M. Eigsti*¹, G. Col-Cozzari², D. Rosset³, D. Da Fonseca³ and C. Deruelle⁴, (1)University of Connecticut, (2)University of Provence, (3)INCM, CNRS; Autism Resource Center, (4)INCM, CNRS

Background: In traditional approaches to cognition, experiences are encoded as abstract symbols, stripped of their perceptual and bases. More recent theories associated with "embodied cognition" approaches suggest that initial sensory, motor, and emotional aspects of experiences have an ongoing impact on cognitive processing. Because a) data from numerous labs suggest subtle difficulties in motor coordination in autism spectrum disorders (ASD), and b) embodied cognition may relate to deficits in emotional contagion and other social processes in ASD, this study examined motor system influences in encoding novel stimuli.

Objectives: To determine whether individuals with ASD display embodiment effects.

Methods: Drawing on the specialized physical systems of approach and avoidance, which allow us efficiently process emotional valence (Darwin, 1872), we contrasted responses to novel visual stimuli that were presented in the context of an approach posture versus an avoidance posture. Fifteen verbal individuals with high-functioning ASD, ages 11-29, age-matched to 15 typically developing (TD) individuals, completed an "embodied" stimulus encoding task. In an *encoding* phase, subjects made "like/don't-like" judgments about neutral Japanese "kanji" characters while maintaining an approach or an avoidance posture. In the *response* phase, subjects chose one of two pictures that best matched the kanji meaning, for the "*approach*" kanji, the "*avoid*" kanji, and *novel* kanji. Image pairs were drawn from the IAPS; for each of 36 pairs, one image was more positive ($M = 7.18$, on a scale of 1 to 9) than the other ($M = 4.99$).

Results: There was a trend for a main effect of condition, $p = 0.09$, suggesting that, across groups, the ratings for kanji initially presented in the Approach condition were significantly higher than ratings for Control kanji, $p = .046$.

Repeated-measures ANOVA also indicated a significant condition by group interaction on stimulus encoding, $p = 0.04$, which reflected the fact that the TD group's ratings for Approach kanji were significantly higher than for Avoid kanji, $p = .01$; their Approach ratings were also significantly higher than their Control kanji ratings, $p = .01$. The ASD group showed no such effect, and indeed tended to evaluate the Avoid kanji *more positively* than the Approach kanji, $p = .09$.

Conclusions: Consistent with prior research, TD individuals showed a significant impact of initial body postures on subsequent, non-postured, evaluations of visual kanji stimuli, such that they evaluated kanji *more positively* when those kanji were initially encountered during an Approach posture. In contrast, the ASD group did not show an effect of posture; if anything, they showed the *opposite* pattern in their responses. The current data are consistent with the hypothesis that there is a reduced influence of body posture on the encoding of novel stimuli, putting aside affective or emotional considerations. Because affective responding reflects the influence of motor systems, a failure of quick, efficient, multiple-modality stimulus mappings could lead to the failure of embodiment effects seen here, and may also be central to more general high-level social and communicative difficulties in ASD.

144.170 170 Cognitive Alterations in Autism Spectrum Disorders (ASD). C. Cantio*¹, S. J. White², J. R. M. Jepsen³, G. F. Madsen⁴ and N. Bilenberg¹, (1)University of Southern Denmark, (2)University College London, (3)Center for Neuropsychiatric Schizophrenia Research, (4)Child and Adolescent Psychiatry, University of Southern Denmark

Background:

Cognitive deficits in children with Autism Spectrum Disorders (ASD) are well known. Still we question whether cognitive subgroups exist and whether cognition is associated with core autistic behaviours and/or psychopathology.

Objectives:

The aim of this study was to look at cognitive subgroups and examine how cognition may be associated with core autistic behaviours.

Methods:

31 children diagnosed with an ASD together with 38 neurotypically developed (NTD) children were all tested with a comprehensive 4-hour neuropsychological battery covering the cognitive domains: Theory of Mind (ToM), Executive Functions (EF) and Central Coherence (CC). All children were aged between 8 and 12 years and had IQs between 75 and 145. Core ASD symptoms were assessed with the ADOS and ADI-R, and comorbid symptoms were rated by parents (CBCL) and teachers (TRF).

Results:

We found that the ASD and NTD groups differed significantly on the ToM-composite and EF-composite but not on the CC-composite. No correlations between these three composites were found. The ASD cases were divided into (relatively) good and poor performers on each of the 3 cognitive composites and these groups were compared. The poor ToM-group (N=20) showed greater parent-reported anxiety and internalizing behaviour but did not differ from the good ToM-group in terms of their ASD symptoms. The poor EF-group (N=9) displayed more severe verbal and non-verbal communication symptoms on the ADI-R, as well as greater difficulties using non-verbal means to regulate social interactions and more severe stereotyped and repetitive motor mannerisms. Surprisingly, this group also presented with fewer conduct problems according to both teacher and parent ratings.

Conclusions:

ToM and EF alterations are characteristic of individuals with ASD and differentiate this population from NTD individuals. However, there also appears to be cognitive heterogeneity within the autism spectrum, with only a proportion of individuals displaying each cognitive abnormality. EF difficulties appear to predict ASD symptoms whilst ToM difficulties predict comorbid symptoms.

144.171 171 Endogenous Spatial Attention: Evidence for Intact Functioning in Adults with Autism. M. A. Grubb^{*1}, M. Behrmann², R. Egan², N. J. Minshew³, M. Carrasco¹ and D. J. Heeger¹, (1)*New York University*, (2)*Carnegie Mellon University*, (3)*University of Pittsburgh*

Background:

Attention allows us to selectively process the vast amount of information with which we are confronted. By focusing on a certain location or aspect of the visual scene, visual attention enables the prioritization of some aspects of information while ignoring others. Previous research on spatial attention in individuals with autism spectrum disorders (ASD) has produced inconsistent results. Some studies have shown attentional deficits in individuals with ASD, purportedly linked to an inability to adequately control the attention field (i.e., the location and spread of visual spatial attention), whereas others have provided evidence for intact functioning. Many different methods have been used to study attention in ASD, and this diversity of approaches may have contributed to the inconsistencies in previous findings.

Objectives:

The primary aim of this project was to test the hypothesis that high-functioning adults with autism exhibit a deficit in controlling the deployment and size of the endogenous (i.e., voluntary) attention field, by applying psychophysical methods that are now standard in the field of attention research.

Methods:

In a series of three experiments, we measured the effect of attention on both performance accuracy and reaction times, with and without spatial uncertainty (i.e., lack of predictability concerning the spatial position of the upcoming stimulus). For typically developing individuals, spatial uncertainty increases the size of the attention field. Here, we adopted a spatial uncertainty manipulation to evaluate whether or not this is also the case for individuals with autism. We measured the spatial distribution of performance accuracies and reaction times to quantify the sizes and locations of the attention field, with and without spatial uncertainty, in a group of high-functioning adults with autism (n=9; 20-40 years, 2 female) and a control group matched for age, full score IQ, and verbal IQ (n=9; 20-36 years, 2 female).

Results:

We observed consistent results in all three experiments. Experiment 1 provided evidence that endogenous spatial attention increases performance accuracy and decreases reaction time in individuals with autism and that these effects are statistically indistinguishable from those seen in a typically developing matched control group. Experiment 2 verified that these attentional benefits remain, even when the task requires rapid deployment of attention, indicating that individuals with autism are not only capable of allocating endogenous spatial attention, but that they can do so as quickly as control participants can. Finally, in Experiment 3, we found that individuals with autism exhibited slower reaction times overall with spatial uncertainty, but that the effects of attention on performance accuracies and reaction times were indistinguishable between individuals with autism and typically developing individuals.

Conclusions:

Voluntary allocation of spatial attention, when measured under tightly controlled experimental conditions, is unaffected in high-functioning adults with autism.

144.172 172 Increased Capacity for Time Perception in Autism Spectrum Disorder. A. Remington^{*1} and N. Lavie²,
(1)*University of Oxford*, (2)*Institute of Cognitive Neuroscience, UCL*

Background:

Previous Autism Spectrum Disorder (ASD) research portrays a mixed picture of attentional abilities with demonstrations of both enhancements (e.g. superior visual search performance) and deficits (e.g. higher distractibility) compared to neurotypical controls.

We have used load theory of attention and cognitive control (e.g. Lavie, 2005) to offer a potential resolution. Load theory states that distractor processing depends on the extent to which a task engages full capacity (in conditions of high load) or leaves spare capacity that 'spills over' resulting in distractor processing. Our previous work suggests that ASD is characterised by an increase in visual perceptual capacity. This enhanced capacity leads to the ability to process additional stimuli, which can manifest both as

increased distractibility (Remington et al 2009) and higher detection sensitivity (Remington et al 2012). Thus our resolution of the previous discrepancies in the literature accounts for the superior performance seen on detection tasks (e.g. visual search; Embedded Figures Task) and the susceptibility to distraction; which we assert comes not from a filtering deficit but from increased perceptual capacity.

Objectives:

Thus far, increased perceptual processing capacity associated with ASD has only been established in the visual domain. Here we examine what effect the enhanced capacity has on another important faculty; namely that of time perception. Does this superiority extend into the temporal domain?

Methods:

Young high functioning adults with ASD and a group of age and IQ-matched controls performed a Rapid Serial Visual Presentation task. A stream of crosses of varying colour and orientation (upright/inverted) was presented and participants were asked to detect either any red cross (low load condition) or upright yellow and inverted green crosses (high load condition). The total duration of each stream was 6 or 12 seconds. Following each stream, participants were required to reproduce the time duration of the stream.

Results:

Our findings indicate that for neurotypical controls, time-estimation ability was reduced under high perceptual load. The young adults with ASD were more accurate than controls for the longer stream duration (12 seconds) and for both durations the accuracy of time estimation in ASD was not reduced by the level of visual perceptual load in the stream.

Conclusions:

These results indicate that increased visual perceptual capacity in ASD confers an advantage in time perception.

Despite some previously reported deficits in short-duration time-perception within the auditory domain (Szelag et al 2004; Gowen & Miall, 2005; Martin et al 2010), our findings demonstrate that under certain conditions (i.e. when visual, rather than auditory processing capacity is loaded) individuals with ASD can outperform typical controls. These findings provide new line of support for our hypothesis of increased perceptual processing capacity in ASD.

This further establishes our resolution regarding increased perceptual capacity, extends the findings to an additional domain and suggests that increased perceptual capacity in ASD may underlie both enhancements and deficits seen within the condition.

144.173 173 Analogical Reasoning in Children with Autism Spectrum Disorder: An Eye-Tracking Study. L. Yi*¹, Z. Chen², E. Tan¹, Y. Fan³ and T. Nishida², (1)*Sun Yat-sen University*, (2)*University of California, Davis*, (3)*Guangzhou Rehabilitation & Research Center for Children with ASD*

Background: Analogical reasoning involves identifying and mapping relational correspondences between entities. Few studies have examined the possible deficits in analogical reasoning although recent findings suggest that the basic ability to engage in analogical reasoning and relational mapping is intact in adults and teenagers with autism (Morsanyi & Holyoak, 2010; Reed, 1996; Scott & Baron-Cohen, 1996). Differences in relational mapping between children with autism spectrum disorder (ASD) and typically developing (TD) children would be predicted by the Weak Central Coherence theory (Frith & Happe, 1994; Happe & Frith, 2006), which posits that in contrast to typical people's engaging in global processing and extracting coherent representations, individuals with autism tend to engage in local, detail-focused processing. Also, given that other theories (Rajendran & Mitchell, 2007) propose that executive functions are typically impaired in children with ASD, and that executive functioning is an important aspect of analogical reasoning (Richland et al, 2010), deficits of analogical reasoning in ASD children are predicted. This study was designed to test, integrate, and extend these theories.

Objectives: The present study was designed to examine the possible differences in analogical

reasoning and relational mapping between ASD and TD children with an eye-tracking approach.

Methods: Eighty-two children participated in four groups: 6- and 8-year-old ASD children and age-matched TD children. The older ASD group and the younger TD group were matched by IQ. All children were tested in a series of relational mapping tasks adopted from Honomichl and Chen (2006): the picture-comparison, object-mapping, and cross-mapping tasks. Children were instructed to view the pictures and solve the problems while their eye movements were recorded. In addition, a series of EF tasks (e.g., Stroop-like tasks and the Flexible Item Selection Task) were also included to assess working memory, flexibility, and inhibition.

Results: The data analyses focused on the possible differences between ASD and TD and developmental differences in the EF measures, the relational mapping performance (based on their verbal report as well as fixation time on the correct and incorrect objects), and children's encoding of the relations between elements in the pictures (as revealed by their eye-movements/paths on the pictures). Analyses with ANOVAs and stepwise regressions reveal the following key findings: 1) TD outperformed ASD in relational mapping tasks in both verbal reports and fixation time; 2) the TD groups were more likely to encode the relations than ASD; TD also outperformed ASD in almost all the EF tasks; 4) developmental differences in these measures were also revealed; and 5) flexibility is a significant predictor for encoding, and IQ and encoding are predictors for relational mapping performance.

Conclusions: These results clearly demonstrate deficits with autism in analogical reasoning, and support the model illustrating the mechanisms involved in relational mapping impairment in autism. Deficits in EF cause the difficulty in identifying and encoding the relations, and this relational encoding impairment is a cause for engaging in the local- elements and perceptually driven features processing instead of global, relational, and structural processing.

144.174 174 The Role of Declarative Memory Process for Children with Low Functioning Autism When Using Personalised Speech Generated Devices. S. J. ni Chuileann*, *Trinity College Dublin*

The role of declarative memory process for children with low functioning autism when using personalised speech generated devices

Background: This study investigates the impact of impairments in declarative memory on the ways children with low-functioning autism (LFA) interact with augmentative and alternative communication (AAC) devices. Recent technological advances in AAC involve attempting to transplant either the natural voice of a minimally verbal child, or a very similar one, onto the device so that the devices' output will sound more like that of the child (The Nancy Lurie Marks Foundation, 2009). The rationale for developing these features on AAC devices is twofold. Firstly, it is assumed that the user will prefer a more naturalistic output resembling human speech to digitised default speech-output. Second, that both the quantity and quality of the individual user's communication via the AAC device will be enhanced through a process of reinforcement on foot of conversational partners' preference for the more naturalistic voice.

Objectives: This first part of this study explores critical components related to voice recognition, levels of familiarity and recollection in a sample of children with LFA compared to age and ability matched control groups. The second part of this study investigates childrens use of personalised speech output options on AAC devices over a three month period.

Methods: Three groups of children were recruited; thirty-three children with LFA, thirty-three typically developing (TD) children matched with the LFA group for non-verbal mental age (NVMA), and twenty-seven children with developmental delay (DD) without autism, matched with the LFA group for chronological age (CA), verbal, and nonverbal ability. An experimental design was used. A series of five tests were conducted to assess voice recognition, levels of familiarity and degrees of recollection across the groups. Based on this data, 12 children with LFA were allocated AAC devices. Language activity monitoring (LAM) software tracked their individual use of the device over a three month period. Analyses undertaken included, tests of

association (correlation), tests of difference (t-tests, ANOVAs), and calculations of effect size.

Results: The analyses in part one showed that children with LFA are significantly impaired in voice processing abilities and in relation to familiarity and recollection relative to DD and TD control groups. This trend remained after controlling for gender, NVMA, schools, and CA. The analyses in part two indicated that personalised speech outputs did not serve to increase or enhance communication in this cohort. Rather than preferential use of the personalised speech output, differential use of speech output was evident with partial and complete abandonment of the devices by a small number of the children.

Conclusions: The combined language and learning deficits in LFA make them ideal candidates for AAC systems however, due to perceptual processing and sociocognitive impairments, additional features such as pre-recorded natural voices on AAC devices may be of no added benefit to this group. Instead a series of short, inexpensive tests can be conducted to match the right system to each individual child with a focus on the child's abilities, preferences, and evolving needs.

499 words

144.175 175 Working Memory and Inhibition in ASD. M. de Vries* and H. M. Geurts, *University of Amsterdam*

Background:

Children with an autism spectrum disorder (ASD) have deficits in working memory (WM) and inhibition. However, studies on WM using the n-back task are inconclusive, partly because of small sample sizes and wide age ranges. The few studies on inhibition using the stop task, a pure measurement of inhibition, are also inconclusive. The only study using a classic stop task showed that children with ASD had an inhibition deficit, but so far this finding has not been replicated. Hence, it is unclear if school age children with ASD show WM deficits when measured with an n-back task, or inhibition deficits when measured with a stop task.

Objectives:

We investigated WM (n-back) and inhibition (stop task) in a large sample of children with ASD. Besides regular group comparisons, we explored if children with ASD that experience WM and/or inhibition deficits showed different symptom severity, behavior, and cognitive ability than children without deficits.

Methods:

Seventy-seven children with ASD (67 male), and 45 typically developing (TD) children (27 male) performed an n-back task, and 74 children with ASD (64 male), and 43 TD children (26 male) performed a stop task (all children were 8-12 years, IQ>80). As the male/female ratio differed between groups, gender was taken into account in analyses. The ADI-R was administered to parents of the ASD group, and all parents filled out the social responsiveness scale, and the disruptive behavior disorder rating scale.

Results:

N-back task accuracy of the ASD group increased more between the 0 and 1-back level than in the TD group, resulting in a worse 1-back level performance in ASD. Groups performed similarly poor at the 2-back level; apparently this level was too difficult for both groups. There were no significant group differences in reaction times.

Children with ASD also performed worse than TD children on the stop task. In both tasks there was no gender effect. Within the ASD group, children with WM and/or inhibition deficits had more conduct and oppositional defiant behavior than children without deficits.

Conclusions:

The ASD group showed both WM and inhibition deficits, but these deficits were not present in all children with ASD. Parents of children with ASD that did show WM and/or inhibition deficits reported more conduct and oppositional defiant behavior than parents of children with no deficits.

Background: It is well established that Autism Spectrum Disorder (ASD) is characterised by a profile of memory strengths and weaknesses that parallels the pattern seen in neuropathologies of the frontal and medial temporal lobes. Specifically, individuals with ASD experience difficulties in recollecting the spatial and temporal relations amongst elements of experience that uniquely define a prior episode, whilst their factual knowledge is relatively preserved (see Boucher et al., 2012). This pattern would predict source memory difficulties in ASD (where, when, how or from whom one has learned something) but the evidence in this context is surprisingly mixed as well as limited. Here we examine source memory systematically under varying task demands to establish whether difficulties in this domain in ASD might relate to task characteristics such as the number of to-be-remembered items and/or the number of to-be-remembered source locations.

Objectives: To establish which task characteristics render source memory experiments difficult for individuals with ASD.

Methods: 10 ASD and 10 typically developing (TD) comparison participants, matched on chronological age, gender and Full-Scale IQ have been tested so far. Each participant completed four versions of a source memory task that varied orthogonally with respect to the number of to-be-remembered items and the number of to-be-remembered source locations. Specifically, either 16 or 32 items were presented in either 4 or 8 locations on the screen. The instructions specified that participants should try to remember the objects as well as the locations at which they appeared on the screen. During test, participants were first asked to decide whether or not they had seen a particular object (33% of objects were new) and if they responded positively they then had to choose the coloured location at which they thought it had appeared during study.

Results: Performance on the item recognition part of the test was above 70% in both groups and a 2 (group) x 2 (4 vs. 8 source locations) x 2 (16 vs. 32 items) ANOVA revealed no main effects or interactions ($p > 0.1$). Source memory was computed as the proportion of correct source identifications for correctly recognised items and an ANOVA of these proportions showed

significantly worse performance in the ASD group ($F(1,18) = 10.41, p < .01$) and significantly worse performance in the 8 as compared to the 4 source location conditions ($F(1,18) = 4.97, p < .05$). A lack of significant interactions suggests that both groups were affected similarly by the experimental manipulations.

Conclusions: Consistent with the broader pattern of memory strengths and weaknesses evident in ASD we observed preserved object recognition but compromised source memory in ASD adults. Both groups responded similarly to manipulations of task difficulty in terms of the number of to-be-remembered items (which had surprisingly little effect in both groups) and the number of to-be-remembered source locations, suggesting that these factors are unlikely to be the source of inconsistent findings in previous studies. Further studies are required to determine what factors might facilitate source memory in ASD.

144.177 177 Attention and Executive Function As Predictors of Functional Impairments in Adolescents with Autism Spectrum Disorder. L. Hall*, E. A. Kelley, D. Wilson, R. Furlano, E. Ladwig and J. Rajsic, *Queen's University*

Background: Executive function (EF) and attention are two cognitive abilities that consist of the fundamental skills necessary for directing and maintaining focus, as well as goal-directed behaviour and problem solving. Such abilities have been found to be critical for the development of functional outcomes such as social skills, academic achievement, and adaptive behaviour. The relationship of attention and EF with functional outcomes is relevant to clinical populations that show deficits in these abilities, such as individuals diagnosed with an autism spectrum disorder (ASD). EF deficits are likely related to many of the commonly reported social, academic, and daily living impairments experienced by individuals with ASD. Clarification is needed regarding the link between these deficits and functional outcomes, especially with respect to adolescents.

Objectives: The current study aims to extend our understanding of these cognitive and functional deficits among adolescents with ASD. Firstly, this study investigates the nature of EF and attention deficits in adolescents with ASD as compared to typically developing (TD) controls. Secondly, this study examines the association of EF and

attention with functional outcomes in adolescents with ASD, as well as in TD controls. Findings will help clarify the nature of the relationship between cognitive and functional deficits in adolescents with ASD.

Methods: We anticipate a sample of 60 adolescents (30 ASD and 30 TD), 12-18 years of age. EF is assessed using five subtests from the Delis-Kaplan Executive Function System (DKEFS). Attention is assessed using four custom attention tasks administered on the computer. Academic ability is assessed using five subtests from the Woodcock-Johnson III Tests of Academic Achievement (WJ-III). Social skills are assessed with the Social Skills Rating System (SSRS) parent report. Adaptive behaviour is assessed with the Vineland Adaptive Behaviour Scale-II (VABS-II) parent survey interview form. Such a battery of assessments allows for cross-informant reports on cognitive and functional abilities.

Results: Preliminary results are based on a sample of 27 participants (6 ASD and 21 TD). Independent samples Mann-Whitney U tests show that the ASD group scores lower than the TD group on a number of cognitive shifting EF tasks at trend level significance ($ps < .07$). However the ASD group only scores lower on one measure of attention ($p = .05$). Additionally, Pearson correlations reveal trend level correlations between cognitive shifting EF tasks and functional outcomes ($ps < .06$), as well as trend level correlations between many measures of attention and functional outcomes ($ps < .07$). Marginally significant results suggest a trend towards significance once a larger sample is collected.

Conclusions: Preliminary findings indicate deficits in EF, academic ability, social skills, and daily living skills in adolescents with ASD. Additionally, lower EF and attention are correlated with higher levels of functional impairment for both ASD and TD groups. Findings will help clarify the nature of the relationship between cognitive and functional deficits in ASD. Insight into these issues may be beneficial for planning intervention and support for these individuals as they mature.

145 ASD and ADHD: Familially Related?
Moderator: H. M. Geurts *University of Amsterdam*

Organizer: A. M. Sluiter-Oerlemans Radboud University Medical Centre Nijmegen, Donders Institute for Brain, Cognition and Behavior, the Netherlands

Autism Spectrum Disorders (ASD) and Attention-Deficit/Hyperactivity Disorder (ADHD) are both highly heritable neuropsychiatric disorders. Together they account for over 50% of the yearly new referrals in child and adolescent psychiatry. There is substantial comorbidity between both disorders, which has received little research attention due to a comorbid diagnosis restriction in the DSM-IV. With the removal of this restriction in the upcoming DSM-5, it is vital to gain more insight in the causes and consequences of a comorbid diagnosis. In this symposium, a series of inventive studies will be presented illustrating to what degree ASD and ADHD (non-)overlap regarding diagnostic information and cognitive profiles, to what extent the low end of the ASD/ADHD spectrum indeed represent superior functioning, if simplex and multiplex families show differential patterns of cognitive problems and to what degree parental ASD/ADHD symptoms influence the family environment in families with ASD/ADHD affected offspring. Strong emphasis will be given on the clinical implications of these findings.

145.001 Are Autism Spectrum Disorders and Attention-Deficit/Hyperactivity Disorder Different Manifestations of One Overarching Disorder? Cognitive and Symptom Evidence From a Clinical and Population Based Sample. J. M. J. Van der Meer*¹, A. M. Oerlemans², D. J. van Steijn², M. G. A. Lappenschaar³, L. M. J. de Sonneville⁴, J. K. Buitelaar⁵ and N. N. J. Rommelse⁶, (1)*Radboud University Medical Centre Nijmegen, Donders Institute for Brain, Cognition and Behavior*, (2)*Karakter Child and Adolescent Psychiatry University Centre Nijmegen*, (3)*Institute for Computing and Information Science, Radboud University*, (4)*Leiden University*, (5)*Radboud University Nijmegen Medical Centre, Donders Institute for Brain, Cognition and Behavior*, (6)*Radboud University Medical Centre, Donders Institute for Brain, Cognition and Behavior*

Background: Autism Spectrum Disorders (ASD) and Attention-Deficit/Hyperactivity Disorder (ADHD) frequently co-occur. Given the heterogeneity of both disorders, several more homogeneous ASD-ADHD comorbidity subgroups may exist.

Objectives: The current study examined if such subgroups exist and whether their overlap or distinctiveness in associated comorbid symptoms and cognitive profiles gave support for a gradient overarching disorder hypothesis or a separate disorders hypothesis.

Methods: Latent class analysis (LCA) was performed on Social Communication Questionnaire (SCQ) and Conners' Parent Rating Scale (CPRS-R:L) data of 644 children (5 to 17 years of age). Classes were compared for

comorbid symptoms and cognitive profiles of motor speed and variability, executive functioning, attention, emotion recognition and detail-focused processing style.

Results: LCA revealed five classes: two without behavioral problems, one with only ADHD-behavior, and two with both clinical symptom levels of ASD and ADHD, but with one domain more prominent than the other ((ADHD(+ASD) and ASD(+ADHD)). In accordance with the gradient overarching disorder hypothesis were the presence of an ADHD class without ASD symptoms, and the absence of an ASD class without ADHD symptoms, as well as cognitive functioning of the simple ADHD-class being less impaired than that of both comorbid classes. In conflict with this hypothesis was that there was some specificity of cognitive deficits across classes.

Conclusions: The overlapping cognitive deficits may be used to further unravel the shared etiological underpinnings of ASD and ADHD, while the non-overlapping deficits may indicate why some children develop ADHD despite their enhanced risk for ASD. The two subtypes of children with both ASD and ADHD behavior will most likely benefit from different clinical approaches.

145.002 Theory of Mind in Children with ASD and Children with ADHD. S. J. M. Kuijper*¹, P. Hendriks², H. M. Geurts³, W. P. M. Van den Wildenberg⁴, B. Hollebrandse² and C. A. Hartman¹, (1)*University of Groningen, University Medical Center Groningen*, (2)*University of Groningen, Center for Language and Cognition Groningen (CLCG)*, (3)*University of Amsterdam*, (4)*University of Amsterdam, Amsterdam Center for the Study of Adaptive Control in Brain and Behaviour (Acacia)*

Background: Children with Autism Spectrum Disorder (ASD) have problems in Theory of Mind (ToM), which is the ability to understand the thoughts, feelings, and perspectives of oneself and others. There are some hints in the literature that this may also be the case for children with ADHD. Both children with ASD and children with ADHD show problems with regulating their behavior (executive functioning).

Objectives: This study investigates the extent to which problems with Theory of Mind also occur in children with ADHD. ToM in ASD and ADHD is

additionally compared with ToM in typically developing children of the same age. In addition, we investigate if response inhibition, working memory and language comprehension serve as mechanisms in understanding ToM problems in children with ASD and ADHD.

Methods: Semi-structured clinical interviews for ASD and ADHD were carried out to confirm diagnosis: ADOS, ADI-R, and PICS. ToM was tested with two "false belief" tasks in children with ASD (n=41), children with ADHD (n=37), and a healthy control group (n=38). Two executive functioning tasks, i.e. a working memory and a response inhibition task, and a language comprehension task were administered to determine if these are possible mechanisms underlying problems with ToM.

Results: Children with ASD and children with ADHD scored similarly low on the ToM tasks. However, the lower scores on ToM in ADHD were partly accounted for by working memory, variability in performance and language comprehension. In contrast, the problems in ToM in ASD persisted if working memory, variability in performance and language comprehension were taken into account. Response inhibition did not mediate ToM performance.

Conclusions: Children with ADHD have problems with ToM, just like children with ASD. However, the mechanisms underlying these ToM problems seem to be different in children with ADHD than in children with ASD. Our findings fit in a growing literature that shows that children with ADHD have social problems, including ToM problems. Even if the mechanisms contributing to social problems in ADHD differ from those in ASD, clinicians need to be aware of and monitor the social problems that are present in this group. ToM problems in ASD cannot be explained by more general EF and language comprehension skills.

Background: Autism Spectrum Disorders (ASD) and Attention-Deficit/Hyperactivity Disorder (ADHD) are both highly heritable neurodevelopmental disorders that frequently co-occur. Research suggests that about 50-70% of the covariance of ASD and ADHD might be explained by shared additive genetic factors. For both disorders, a polygenic mode of inheritance has been proposed in most cases, supported by findings that similar (yet milder) abnormalities are present in unaffected relatives who carry susceptibility genes for the disorder. However, in some families in which ASD or ADHD affects only one individual in the family (simplex families), it is likely that causal factors not shared between family members (such as rare single gene mutations or CNVs) may play a role. Therefore, we hypothesize that unaffected siblings from ASD and ADHD multiplex families, but not simplex families, display (mild) cognitive deficits similar to their ASD/ADHD affected sibling and have elevated levels of ASD (in ADHD cohort) and ADHD (in ASD cohort) symptoms.

Objectives: This study has two main objectives: (1) to examine if the etiology is indeed different in simplex versus multiplex families based on cognitive and symptom presentation of unaffected siblings and (2) whether ASD and ADHD share etiological underpinnings based on overlap of cognitive problems in ASD and ADHD affected children and increased symptoms of ASD in relatives of ADHD multiplex probands and vice versa.

Methods: The current study used a large sample of simplex and multiplex families from two family-genetic cohorts. A total of 186 ASD families (431 children), 184 ADHD families (545 children) and 209 control families (414 children) were included. Multiplex families were defined as two or more ASD affected individuals in ASD families and two or more ADHD affected individuals in ADHD families. Simplex families were required to have a single-affected child and a minimum of one male unaffected sibling. Several cognitive domains were examined, such as executive functions, social cognition, motor function, and central coherence.

145.003 Evidence for Cognitive Endophenotypes in Multiplex, but Not Simplex ASD and ADHD Families? A Focus On Unaffected Siblings. A. M. Oerlemans^{*1}, Y. G. E. De Bruijn¹, D. J. van Steijn¹, B. Franke², J. K. Buitelaar³ and N. N. J. Rommelse², (1)Karakter Child and Adolescent Psychiatry University Centre Nijmegen, (2)Radboud University Medical Centre, Donders Institute for Brain, Cognition and Behavior,

Results: We are currently in to process of running our analyses. We plan on conducting linear mixed models to examine group differences on neuropsychological measures and symptom presentation in children with ASD and ADHD and their unaffected siblings. Groups will be defined as: (1) affected children vs. unaffected siblings vs. controls (analyses separate for ASD and ADHD cohort), (2) affected children from simplex families vs. affected children from multiplex families vs. controls, (3) unaffected siblings from simplex families vs. unaffected siblings from multiplex families vs. controls, (4) ASD affected children vs. ADHD affected children vs. controls, and (5) ASD unaffected siblings vs. ADHD unaffected siblings vs. controls.

Conclusions: This is the first study to examine differences in cognitive performances and behavioral symptoms between simplex and multiplex families in both ASD and ADHD families. We expect to find (mild) cognitive impairments and higher rates of comorbid ASD or ADHD symptoms in unaffected siblings from multiplex, but not simplex families. Our findings may provide new insights into the mechanisms of inheritance and the shared etiological underpinnings of ASD and ADHD.

145.004 Are Autism Spectrum Disorders and/or Attention-Deficit/Hyperactivity Disorder Symptoms Related to Parenting Styles in Families with ASD (+ADHD) Affected Children?.
D. J. van Steijn*¹, A. M. Oerlemans¹, S. W. de Ruiter², M. A. van Aken³, J. K. Buitelaar⁴ and N. N. J. Rommelse²,
(1)*Karakter Child and Adolescent Psychiatry University Centre Nijmegen*, (2)*Radboud University Medical Centre, Donders Institute for Brain, Cognition and Behavior*, (3)*Department of Developmental Psychology, University Utrecht*, (4)*Radboud University Nijmegen Medical Centre, Donders Institute for Brain, Cognition and Behavior*

Background: An understudied and sensitive topic nowadays is that even subthreshold symptoms of Autism Spectrum Disorder (ASD) and Attention-Deficit/Hyperactivity Disorder (ADHD) in parents may relate to their parenting styles.

Objectives: The aim of this study was to explore whether suboptimal parenting styles exist in families with a child with ASD (+ADHD) and to what extent these were related to parent and/or offspring symptoms.

Methods: 96 families were recruited with one child (2-20 years) with a clinical ASD (+ADHD) diagnosis, and one unaffected sibling. Parental ASD and ADHD symptoms were assessed using self-reports. The Parenting Styles Dimensions Questionnaire (PSDQ) self- and spouse report were used to measure the authoritative, authoritarian and permissive parenting styles.

Results: Fathers and mothers scored significantly higher than the norm on the permissive, and lower on the authoritative and authoritarian parenting style for affected and unaffected children. Self- and spouse report correlated moderately to highly. Higher levels of paternal and maternal ADHD symptoms were related to suboptimal scores to almost all parenting styles. Further, an interaction effect was found, indicating that mothers with high ASD symptoms reported to use a more permissive parenting style only towards their unaffected child.

Conclusions: In ASD (+ADHD) families, parents report to use a less optimal parenting style. This appeared true for both fathers and mothers, was mostly unrelated to the diagnosis of the child, but primarily to parental self-reported ADHD and less to ASD symptoms. Parenting training in ASD (+ADHD) families may be beneficial for the well being of both parents and their offspring.

146 Novel Methods and Paradigms for Studying Early Autism: A European Perspective

Moderator: H. Roeyers Ghent University

Organizer: H. Roeyers Ghent University

ESSEA (Enhancing the Scientific Study of Early Autism) is a network of scientists from 22 countries, funded by the European Cooperation in Science and Technology (EU-COST). One important goal of this network is to develop and advance novel methods for studying autism in young children and infants. It is essential for the scientific study of early autism that expertise in advanced methods for studying perception, cognition, and brain function is shared and broadened, that particular protocols are being developed that can be run at multiple sites and that data can be pooled. Technologies being used in the participating labs include electroencephalography (EEG), (live) eye-tracking, skin conductance responses and heart rate monitoring. This scientific panel will report on paradigm developments in Europe and will demonstrate their added value by providing new and compelling empirical findings in children with autism and in high-risk siblings. Implications for early autism research will be discussed.

146.001 Typical Orienting but Impaired Processing of Social Information in Infants At-Risk for ASD. T. Gliga*¹, M.

Elsabbagh², R. Bedford³, T. Charman⁴, M. H. Johnson¹ and ..
The BASIS Team⁵, (1)*Birkbeck, University of London*,
(2)*McGill University*, (3)*Institute of Psychiatry*, (4)*Institute of Education*, (5)*BASIS*

Background: Developmental theories of autism spectrum disorders (ASD) can be broadly divided into those that see the social and communication difficulties as emerging from impairments in *processing* social information (Baron-Cohen, Leslie & Frith, 1985; Gliga et al, 2012) and those that propose they stem from an inability to *orient* to or *attend* to the social world (Dawson et al., 2004; Chevalier et al, 2012). According to the second account diminished early "social" orienting biases, for example, would limit the exposure to social interaction and have cascading effects on learning from and about people. These orienting mechanisms are subserved by evolutionarily conserved (Shepherd, 2010) sub-cortical and cortical structures (Johnson, 2005) that are functional from very early in life in typical development. Prospective studies of infants at-risk for ASD offer the ideal opportunity for testing they are impaired very earlier in development in ASD.

Objectives: We present emerging findings from the British Autism Study of Infant Siblings (BASIS; <http://www.basisnetwork.org/>) investigating the ability to orient to and engage with a variety of "social" stimuli, during the first year of life.

Methods: We have used an eye-tracker (Tobii) to measure infant's ability to (1) orient to faces presented amongst other distractors, in a static visual search display (Elsabbagh et al, 2012); (2) orient to eye, mouth or hand movements and (3) to follow someone's head and eye gaze to a proximal object (Bedford et al, 2012). Fifty-four infants at high risk for ASD (because of having an older sibling with the disorder) and 50 infants with no family history of ASD, therefore at low risk, took part in a longitudinal study. Infants were seen at 7 and 13 months of age and then again after their 3rd birthday. Following a clinical assessment at the latter age high-risk siblings were classified as having developed ASD (HR-ASD), other atypicalities (HR-Aty) or no atypicalities (HR-TD).

Results: We found no evidence for difficulties with orienting to faces, eyes or human actions in infants that later developed an ASD. At all ages

HR-ASD oriented to faces and remained engaged with them to the same extent as the other HR or LR participants. HR-ASD showed no difficulties orienting to the eyes of a face in a static display or to eye, mouth or hand movements. No difference was found between groups in terms of correctly following someone's gaze. However subtle differences appeared when analyzing the amount of time infants spent looking at someone's object of interest, in the gaze following study.

Conclusions: Across three eye-tracking studies we found little evidence for an impairment in "social orienting" biases during the first year of life in those infants that go on to develop an ASD. These results agree with previous findings of gradual decrease in social engagement later during childhood (Swettenham et al, 2003; Chawarska et al, 2009) possibly as a result of earlier difficulties with processing social information, e.g. difficulties understanding the communicative function of social cues like gaze and head shifts.

146.002 Mirror Neuron Functioning in Young Children with or At Risk for ASD. P. Warreyn*, L. Ruyschaert, J. R. Wiersema and H. Roeyers, *Ghent University*

Background:

Human mirror neurons have theoretically been linked to imitation, language, empathy, and other social-communicative skills. Since most of these skills are impaired or delayed in children with autism spectrum disorder (ASD), it has been hypothesized that the mirror neuron system may be dysfunctional in individuals with ASD. Although this 'broken mirror' hypothesis was confirmed in some studies, others found evidence for a normally functioning mirror neuron system in ASD. Although mirror neurons are highly influenced by (social and motor) experience, until now no studies were conducted with infants or young children with ASD. It may however be expected that while children with ASD grow older, the limited amount of social information they process may hamper the development of a fully functional mirror neuron system.

Objectives:

To investigate mirror neuron functioning in typically developing young children, in young

children with a diagnosis of ASD, and in young children with an elevated risk for ASD (defined by having at least one older sibling with ASD).

Methods:

We used EEG mu suppression as an index of mirror neuron functioning. Sufficient artefact-free EEG data was obtained from 33 typically developing children, 24 children with ASD and 25 siblings of children with ASD (mean age = 42 months, SD = 15). Mu suppression was measured in three conditions, relative to a baseline. In these conditions, the children 1) observed intransitive hand movements, 2) observed actions on objects or 3) were invited to imitate the actions on objects. During the baseline, they only observed moving objects.

Results:

On the central electrode positions C3 and C4, we measured significant mu suppression in the three conditions, in all three groups. A repeated measures MANOVA showed no main effect of group and no group*condition interaction effect. During the imitation condition, the mu suppression in all three groups tended to be stronger than in the other two conditions. Although mu suppression in all three conditions was strongly intercorrelated, there were no correlations between mu suppression on the one hand and child characteristics such as age, language level, imitation score and autism symptoms on the other hand.

Conclusions:

In young children with or at risk for ASD, we found a functional mirror neuron system, as measured by mu suppression. Together with the absence of correlations between mu suppression and social communicative abilities, these results do not provide evidence for the 'broken mirror' hypothesis.

146.003 Altered Modulation by Communicative Signals On Cognitive Performance in Children with Autism. T. Falck-Ytter^{*1}, C. Carlström² and M. Johansson², (1)Center of Neurodevelopmental Disorders at Karolinska Institutet (KIND), (2)Uppsala University

Background: In typical development, eye contact facilitates performance on specific socio-cognitive tasks. For example, typically developing infants tend to process others' communicative signals more accurately if preceded by direct gaze, signaling that the infant is the intended addressee. Preliminary evidence suggests that eye contact may be less beneficial for children with Autism Spectrum Disorder (ASD).

Objectives: Here we asked whether facilitation could be observed in typically developing children during non-social cognitive tasks. Moreover, we predicted that modulation by communicative signals on cognitive performance would be altered in children with ASD.

Methods: We assessed the ability of neurotypical children (n = 27) and children with ASD (n = 12) to repeat series of digits in a modified digit span task adapted from a gold standard and widely used intelligence test. The children were 4 to 10 years old, and the groups were matched on full scale IQ. The test administrator, sitting in front of the child, first established the child's maximum digit span by gradually increasing the difficulty of the task. When established, series of difficult (the child's maximum digit span) and easy (2 digits) trials were given in blocks of four. On every second trial the administrator either looked at the child (the gaze condition) or looked down towards the test protocol (the no-gaze condition). Performance during difficult trials was evaluated as a function of group and condition. In addition, we measured the children's eye movements during the task to evaluate attentional differences, using live eye-tracking (Tobii TX300).

Results: As predicted, we observed a differential modulation of the gaze/no-gaze manipulation on performance (digit span) in the two groups ($p < .05$). Direct gaze increased performance in typically developing children but not in children with ASD. Live eye-tracking data showed that both groups looked away from the face of the test administrator during thinking and answering phases of the interaction.

Conclusions: This study suggests that in typical development, positive effects of eye contact can be observed even outside the socio-cognitive domain. Moreover, it indicates that eye-contact is less beneficial for children with ASD than for

children with typical development. The eye-movement data suggest that both groups modulated their eye contact adaptively as a function of the task demands. In addition to their potential clinical significance, the results have implications for our understanding of the interplay between social context and cognition in ASD during the first years of life.

146.004 Psychophysiological Responses to Direct Gaze in Children with Autism Spectrum Disorder. A. Kylläinen^{*1}, S. B. Wallace², A. J. Bailey³ and J. K. Hietanen¹, (1)University of Tampere, (2)Autistica, (3)UBC

Background: It remains unclear why children with autism spectrum disorder (ASD) tend not to look at the eyes of other people. It has been suggested that direct gaze elicits an unusual degree of psychophysiological arousal that is felt uncomfortable by children with ASD. An alternative suggestion is that direct gaze is not socially motivating and, therefore, ASD children passively ignore it.

Objectives: The aims of the study were to investigate psychophysiological arousal and motivational brain responses to direct gaze in children with ASD. Skin conductance responses (SCRs), heart rate acceleration, and frontal alpha-band EEG activity were measured. Relative left- and right-sided asymmetries in the frontal alpha-band EEG activity have been associated with activation of the approach- and avoidance-related motivational brain systems, respectively.

Methods: The participants included 14 children with ASD and 15 gender-, age- and IQ-matched controls. The children ranged from 11 to 14 years old. The children viewed pictures of three familiar (parents and a teacher) and three unfamiliar faces with eyes shut and eyes open with a direct gaze. The stimuli were presented so that they first loomed toward the participants, creating an impression of an approaching person. The stimuli loomed for 3 seconds and then were static for 2 seconds. Skin conductance, electrocardiogram, and frontal EEG activity were recorded simultaneously.

Results: The results showed that the ASD children had greater SCRs to direct gaze compared to shut eyes, whereas in the typically developing children there was no difference

between the gaze conditions. Typically developing children viewing faces with direct gaze showed greater relative left-sided, approach-related frontal EEG activity than when viewing faces with eyes shut. In children with ASD, the eye condition (direct gaze vs. shut eyes) did not have an effect on the frontal EEG activity.

Conclusions: The findings of the study showed that direct gaze elicits enhanced arousal in children with ASD. We could not, however, find evidence that heightened arousal to direct gaze is associated with avoidance tendency. Instead, it seems that children with ASD may lack the typical approach-related response to direct gaze. These findings are in line with assumptions that having eye contact with another person is not socially motivating for children with autism. These findings will be further discussed in relation to ongoing studies in young children with autism.

The study was funded by Autism Speaks and the Academy of Finland.

147 From Genes to Behavior: Translational Approaches Towards a Mechanistic Understanding of Insistence On Sameness (IS) in Autism Spectrum Disorders (ASD)

Moderator: M. W. Mosconi University of Texas Southwestern Medical Center

Organizer: M. W. Mosconi University of Texas Southwestern Medical Center

The insistence on sameness (IS) commonly exhibited by individuals with autism spectrum disorder (ASD) represents a disabling feature that is only minimally affected by current treatments. Its underlying biology is not well understood, but multiple lines of evidence implicate serotonergic (5HT) alterations and frontostriatal dysfunctions. Still, efforts to develop improved and more individualized therapeutic approaches for IS have been constrained by a lack of knowledge about mechanisms bridging genetic alterations to neural system and behavioral aspects. The proposed talks aim to A) characterize the molecular, biochemical, neural system and cognitive bases of IS, and B) integrate knowledge across these levels of analysis to propose directions for future research on the etiology and treatment of these behaviors. This panel will examine 1) gene networks related to IS, 2) rare genetic variants associated with hyperserotonemia (i.e., elevated levels of platelet 5HT) and repetitive behaviors, 3) rodent behavioral pharmacology studies that utilize in vivo brain measurements of 5HT, and 4) clinical studies of neurocognitive and brain system abnormalities associated with IS. We will also discuss some of the challenges inherent in integrating these types of translational efforts and in generating biomarkers and outcome measures for clinical intervention research.

147.001 Neurocognitive Deficits Underlying Insistence On Sameness in Autism Spectrum Disorders (ASD). M. W. Mosconi^{*1}, M. E. Ragozzino², L. M. Schmitt¹, E. H. Cook³ and J. A. Sweeney¹, (1)University of Texas Southwestern Medical Center, (2)University of Illinois at Chicago, (3)University of Illinois at Chicago

Background: Individuals with Autism Spectrum Disorder (ASD) frequently show a rigid adherence to a rule or routine, or an Insistence on Sameness (IS). The neurocognitive alterations that underlie IS behaviors are not well understood. We have recently shown that individuals with ASD often fail to inhibit prepotent responses, suggesting dysfunction of frontostriatal brain systems that may limit affected individuals' ability to interrupt behavioral routines.

Objectives: To determine whether individuals show inhibitory control deficits on a novel stop-signal task, and to examine the relationship of stopping errors and clinically-rated IS behaviors.

Methods: Forty-five individuals with ASD and 40 healthy controls matched on age (range 6-38 years) and Performance IQ were administered manual motor and oculomotor stop-signal tasks (SST) and baseline measures of reaction time. During the SST, subjects 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 following the appearance of the peripheral cue ('STOP' trials). We examined subjects' reaction times during both baseline and SST GO trials, as well as the rate at which they failed STOP trials (i.e., they pressed a button or looked towards the peripheral target).

Results: Subjects with ASD made more STOP trial errors than healthy controls during manual motor and oculomotor SST ($p < .05$). For individuals with ASD, increased STOP trial error rates were related to increased rates of IS behaviors ($p < .05$). STOP trial error rates also were associated with the degree to which subjects slowed their reaction times from baseline to task GO trials, such that increased slowing was associated with fewer STOP trial errors ($p < .01$). Subjects with ASD did not slow their reaction times as much as controls ($p < .05$). Increased age was associated with fewer STOP trial errors and increased slowing of reaction

times in healthy controls ($p < .01$), but not in subjects with ASD.

Conclusions: These results indicate that individuals with ASD show inhibitory control deficits that are associated with the severity of their IS behaviors. From a neurocognitive perspective, IS appears to reflect, at least in part, a reduced ability to suppress unwanted or context inappropriate responses. This impairment involves a failure to strategically slow behavioral reaction times in order to optimize the capacity to stop these responses when cued. Inhibiting unwanted behaviors involves frontostriatal suppression of the motor pathways that support volitional action. The application of strategic timing biases during SST performance has been shown to recruit medial prefrontal cortices including supplementary motor cortex and supplementary eye fields. Our findings suggest that the development of frontostriatal and medial prefrontal brain systems underlying response inhibition may be disrupted during childhood and adolescence in ASD. Future treatments targeting the biological mechanisms underlying these behaviors therefore may be able to continue advancing behavioral abilities through adolescence and early adulthood even after early emerging impairments have been established in affected individuals.

147.002 The BTBR Mouse As a Translational Model to Understand the Mechanisms Underlying Repetitive Behaviors in Autism. M. E. Ragozzino*, University of Illinois at Chicago

Background:

Restricted interests and repetitive behaviors represents one of the cardinal features of autism spectrum disorder (ASD). Recent findings indicate that individuals with ASD can flexibly reverse learned response patterns when accurate feedback is provided, but are impaired when feedback is provided in a probabilistic fashion. Comparably, BTBR mice, used as a model of idiopathic ASD, exhibit a strikingly similar deficit in probabilistic reversal learning. Both dopamine and serotonin signaling in the striatum have been shown to affect behavioral flexibility and may represent potential neurochemical systems to target for treating behavioral inflexibility.

Objectives:

The objectives of the present experiments were as follows: 1) determine whether the atypical antipsychotic, risperidone selective serotonin 2A receptor antagonist, M100907 or dopamine D2 receptor antagonist, sulpiride attenuates a probabilistic reversal learning deficit in BTBR mice compared to that of C57 mice; 2) determine whether serotonin output in the dorsomedial striatum changes during probabilistic reversal learning in BTBR and C57 mice.

Methods:

In all experiments, mice were food restricted to 85% of their *ad libitum* body weight and trained in a spatial discrimination test. In this spatial discrimination test, mice were tested across two consecutive daily sessions. Mice had to discriminate between two spatial locations in which one location was associated with a food reward on 80% trials and the other location contained a food reward on 20% of trials. In the acquisition test, mice learned to select one spatial location in which a food reward was provided on 80% of trials. The following day, the reinforcement probabilities for spatial locations were reversed and a mouse learned to choose the opposite location as on acquisition. Learning criterion in both test sessions was 6 consecutive correct trials. To measure serotonin output during probabilistic reversal learning, mice were prepared for in vivo microdialysis collection in which a probe was placed in the dorsomedial striatum. Following baseline collection, mice were placed in the maze for reversal learning testing while microdialysis samples were collected at 10 min intervals. All samples were measured using HPLC.

Results: The results indicate that risperidone attenuates the probabilistic reversal learning deficit in BTBR mice in a dose-dependent fashion. M100907 also attenuated the reversal learning deficit in BTBR mice. In contrast, initial findings indicate that sulpiride does not attenuate a reversal learning deficit in BTBR. None of the treatments affected performance in C57 mice. Moreover, initial results indicate that serotonin output increases during reversal learning in C57 mice, but is reduced in BTBR mice.

Conclusions:

The present findings suggest that treatments that selectively target the serotonin 2A receptor, but not the dopamine D2 receptor, alleviate behavioral inflexibility deficits in a mouse model of ASD. Further, dampened serotonin signaling in the dorsomedial striatum may contribute to behavioral inflexibility deficits in BTBR mice. Blockade of serotonin 2A receptors may alleviate behavioral flexibility deficits by enhancing serotonin release in the striatum and may be an effective treatment to reduce restricted interests and repetitive behaviors in ASD.

147.003 Sameness or Difference: Studies in a Genetic Mouse Model of Autism with Hyperserotonemia. C. L. Muller*, T. M. Kerr, R. D. Blakely and J. Veenstra-Vander Weele, *Vanderbilt University*

Background: Elevated whole blood serotonin (5-HT) is the most consistent and heritable biomarker in autism spectrum disorder (ASD). Linkage studies implicate the chromosome 17q11 gene region containing the serotonin transporter (SERT) gene SLC6A4 in males with ASD. Multiple rare SERT variants were identified in families with linkage to this region. The most common of these, Gly56Ala, was specifically associated with rigid-compulsive traits and sensory aversion. We constructed mice that express this SERT Ala56 variant and identified multiple phenotypes, including elevated whole blood 5-HT, increased 5-HT clearance, changes in brain 5-HT homeostasis, and altered social, communication, and repetitive behavior.

Objectives: 1) Extend studies of SERT Ala56 knock-in mice into a second inbred strain, C57BL/6, to evaluate penetrance of observed phenotypes across genetic backgrounds; 2) Evaluate behavioral rigidity in SERT Ala56 mice on a probabilistic reversal learning task that models the behavioral trait of insistence on sameness. 3) Assess the development of the somatosensory system in SERT Ala56 mice.

Methods: SERT Ala56 mice on a 129S genetic background were crossed 10 generations to C57BL/6 mice. Genetic markers were used to establish 99% congenic status. Separately, the native 129S6 SERT was crossed 10 generations to C57BL/6 to establish appropriate control for strain-dependent variation in the SERT gene. Measures of social, communication, and repetitive behavior were used to assess penetrance of

observed phenotypes. Sensitivity to serotonin receptor agonists was also measured to assess impact of this variant on brain 5-HT homeostasis in the C57BL/6 background. Finally, assessment of probabilistic reversal learning and sensory development are underway.

Results: Variable penetrance of the SERT Ala56 variant was seen for different phenotypes across inbred strains. Consistent with previous findings in the 129S mice, SERT Ala56 mice on the C57BL/6 background were more likely to back out on the tube test for dominance when confronted with a control animal ($P < 0.01$). In contrast to the 129S background, no difference between genotypes was observed on the three-chamber sociability test or in hanging behavior in the home cage. At postnatal day 7, C57BL/6 SERT Ala56 pups showed increased vocalizations when separated from the dam ($P < 0.05$), which is opposite to the phenotype observed in the 129S background. Sensitivity to serotonin 5-HT_{1A} and 5-HT_{2A} receptor agonists was not significantly different between SERT Ala56 mice and controls on the C57BL/6 background. Results from objectives 2 and 3 will also be presented.

Conclusions: Variable penetrance of SERT Ala56 phenotypes across genetic backgrounds is consistent with observations in families segregating this variant, where some but not all individuals with the variant share a diagnosis of autism. These results also parallel findings in other genetic mouse models of autism, including the Fmr1 knockout mouse, which shows variable penetrance of behavioral phenotypes across inbred strains. Genetic differences between 129S and C57BL/6 inbred strains may include gene variants that modify sensitivity of the 5-HT system to SERT variation. Other manipulations of the 5-HT system impact probabilistic reversal learning and development of the somatosensory system in mice, but increased SERT function has not previously been examined.

147.004 Hyperserotonemia: Deciphering Genetic Risk Using the Oldest Biomarker in Autism. J. S. Sutcliffe^{*1}, L. K. Davis², E. L. Crawford¹, E. Kistner-Griffin³, N. G. Campbell¹, H. C. Prasad¹, S. J. Guter⁴, B. Li¹, R. D. Blakely¹, N. J. Cox² and E. H. Cook⁵, (1)Vanderbilt University, (2)University of Chicago, (3)Medical University of South Carolina, (4)University of Illinois at Chicago, (5)University of Illinois at Chicago

Background: Multiple lines of investigation implicate serotonergic dysfunction as an etiological factor in ASD. Neurochemistry, neuroimaging of serotonin (5HT) synthesis, tryptophan depletion, 5HT agonist stimulation, and efficacy of potent 5HT transporter (SERT) inhibitors all support this "serotonin hypothesis". While highly genetic, the architecture of genetic risk is highly complex, involving hundreds of genes, with both rare (inherited and de novo) and common variants contributing to overall risk. We focus on the serotonin system as an approach to tease apart ASD genetic liability armed with subject serotonin levels in blood as a biomarker to inform diverse genetic studies.

Objectives: To identify ASD genetic risk factors and that subset acting to influence development and regulation of the serotonin system as evidenced by high levels of 5HT in ~35% of cases.

Methods: We assembled a wide range of genetic and statistical techniques to analyze our ACE cohort, in addition to larger existing samples that permit identification of risk loci using novel approaches with greater power. We recruited, phenotyped and determined blood [5HT] for more than 250 families. Genotyping and Sanger sequencing was conducted for loci most central to serotonin regulation. Select families with hyperserotonemic probands were used for whole exome sequencing (WES) to reveal novel *de novo* and inherited variants that in turn point to networks or pathway relationships, and specific molecules that contribute to both hyperserotonemia and ASD risk. Novel SERT coding variants were functionally assayed to test for effects on activity and regulation. We used larger datasets to test for potential enrichment of (expression) eQTLs and (methylation) mQTLs amongst the most associated loci, along with recent efforts to test for the ability of common variation to account *globally* for ASD liability and eventually variance in blood serotonin levels. CNV analyses were conducted by genotyping probands on high-density Illumina SNP arrays, and CNV prediction conducted using CNVision, which combines multiple algorithms to increase predictive value of CNV calls. Putative CNVs were validated by qPCR in the entire family to determine de novo or inherited status.

Results: We detected two novel functional coding variants in SERT, one of which displayed elevated activity and related phosphorylation and constitutive activation of p38MAP kinase, a critical regulator of SERT. Another variant showed hypomorphic function. Analysis of *de novo* and inherited variants from WES of hyperserotonemic families has putatively identified molecular pathways such as integrin signaling, extracellular matrix (ECM)-receptor interactions, and focal adhesion as important functions contributing to serotonin-related risk factors in ASD. Numerous CNVs have been identified, and these both reinforce known risk loci and nominate new genes as being ASD risk factors. Using large ASD datasets, we observed a significant enrichment of brain eQTLs amongst the most ASD-associated genes.

Conclusions: The sum of our findings continues to highlight the 5HT system as being an important in harboring ASD risk loci, and that discovery from exome sequence and other data will permit us to better understand ASD risk factors, their interrelationships and that subset that relates to the role of dysregulated 5HT signaling in ASD risk.

148 30-Year Follow-Up of Autism in Adulthood

Moderator: M. Farley University of Utah

Organizer: M. Farley University of Utah

The population of adults with ASD is increasing rapidly, entering systems of healthcare and adult support that are already at capacity. Understanding the nature of ASD in adults, their unique needs, and availability of service options, is essential for resource planning and service development. Investigations into this period of life are increasing, but much remains unknown. This study examines adult outcomes for a large, population-based sample of adults identified as children in the 1980's. Outcomes of interest concern diagnostic presentation, functional abilities, co-occurring medical and psychiatric conditions, social functioning, independence, service use, and access to services. Overall, outcomes for this sample were consistent with what has been reported for similar samples, yet there were notable differences in factors contributing to outcomes compared to what has been reported for other groups. Our findings support the importance of a range of accessible healthcare and support service options for adults with ASD. Detailed analyses are underway to investigate patterns leading to specific outcomes for subgroups of the population of adults with ASD.

148.001 Social Functioning of Adults with ASD: Results From a 30-Year Follow-up. M. Farley*¹, W. M. McMahon¹, H. Coon¹, J. Viskochil², S. Harward¹, E. Haygeman¹, A. V. Bakian¹ and D. Bilder¹, (1)University of Utah, (2)Utah Autism Research Program

Background: The Epidemiological Survey of Autism in Utah was a statewide effort from 1984 to 1988 to ascertain all cases of ASD, aged 3 to 25. DSM-IV diagnostic criteria were recently applied to cases of individuals who showed characteristics of ASD during the 1980's study but did not meet DSM-III criteria for Autistic Disorder. The resulting sample from both projects includes 305 adults.

Objectives: To describe the current life situation for a population-based sample of adults with ASD, including level of functional abilities, residential status, service use, and social participation.

Methods: Direct assessments with participants included the ADOS and IQ tests. Informants provided information on social participation, employment, residential history, service use, interests, and requisite levels of support. A social functioning composite score was assigned to each participant reflecting their current residential situation, employment, and social relationships. These scores fall within categories ranging from "Very Good" to "Very Poor".

Results: Adult outcome data have been collected for 63% of the total sample. Participants in the adult assessment included 37 females and 154 males, with an average age of 34.75 years (SD = 6.23 years). Thirty-three were deceased. Social functioning composite scores among the survivors included 21% in the Very Good/Good range, 35% in the "Fair" range, and 49% in the "Poor/Very Poor" range.

Roughly 60% of the participants were unable to complete a standard IQ test for adults. The average Full Scale IQ score for those who completed the test was 72.08 (SD = 28.50).

Employment results were: 15% in full-time work, 24% in part-time work, 24% in supported work or a sheltered workshop, 19% in a day program, and 13% being without any structured daytime activities. Approximately 80% were receiving disability payments and Medicaid.

Results concerning living situation were: 40% living at home with their parents, 8% living in their own homes independently, 5% living in their own homes with regular assistance, 20% living in

a group home, and 26% living in a residential facility that provides constant care and supervision.

Informants reported on participants' interest in having more social relationship, indicating that they believed 68% would not enjoy additional social relationships and 31% would. Informants for 14% said they were uncertain. Roughly 30% of the participants had dated in the past.

Conclusions: Social functioning composite scores for this sample, which includes individuals across the full range of intellectual and functional abilities, were similar to what has been reported for other adult samples. Fewer adults were living with their family of origin than has been reported from previous studies, and a larger proportion was employed than has been reported for other samples. These differences could be related to the fact that this sample is 5 years older, on average, than other samples previously described. Additional years may provide more opportunity to find employment. Others may have become eligible for scarce public resources and entered supportive programs. Aging caregivers may also have acted to move their family member with ASD into adult support services.

148.002 Comorbid Medical Conditions in a Population-Based Sample of Adults with ASD. W. M. McMahon^{*1}, A. V. Bakian¹, J. Viskochil², H. Coon¹, M. Farley¹, E. L. Botts³ and D. Bilder¹, (1)*University of Utah*, (2)*Utah Autism Research Program*, (3)*Vanderbilt University*

Background: Understanding the presence of comorbid medical disorders has important implications for our understanding of adult outcomes and medical care for individuals with autism spectrum disorders (ASD). Several studies have found high rates of co-morbid medical conditions among children and adults with ASD even when compared to individuals with other developmental disabilities. Common conditions include seizures, sleep disturbance, obesity, gastrointestinal symptoms, and endocrine abnormalities. Unfortunately, the frequencies of these conditions or symptoms have not yet been established in a representative sample of adults. Thus, a detailed assessment of current and chronic medical symptoms and conditions provides an important contribution to our

understanding of adult outcomes associated with ASD.

Objectives: This study examines adults with ASD to (1) determine the presence of co-morbid medical symptoms and disorders and (2) identify the patterns of medical symptoms and disorders affecting this population-based adult ASD sample.

Methods: As part of a large adult outcomes study, individuals with ASD (and their caregivers) ascertained during a 1980's state-wide Utah autism epidemiological study reported their medical history and current complaints during a medical review of systems interview. This interview followed a standard medical review of systems approach querying common medical complaints. Further elaboration was obtained for medical conditions which were perceived by the individual and/or caregiver as problematic and/or necessitated intervention. This interview was administered to 82 participants with either DSM III autism [N= 62 (75.3%)] identified in the original study or DSM-IV-TR autism spectrum disorder [N= 20 (24.4%)], identified during a reclassification study. Assessments with caregivers on an additional 10 individuals who were deceased at the time of the follow-up study were also performed.

Results: Assessments were completed on 92 individuals (69 male, 23 female, median age among living participants was 36.1 years, age range 27 to 54, 21 participants had an IQ >69). Median BMI among all individuals was 25.8 with a range of 13.6-59.4. Weight categories were: 13 (19.4%) underweight (BMI<20); 12 (17.9%) normal (BMI 20-25); 17 (25%) overweight (BMI, 25.1-29.9), and 25 (37%) obese (BMI>30). Genetic disorders were present in 13 (14%) of participants (6, 60% of deceased), 17 (18%) individuals were taking medication for at least one chronic medical condition, and 23 (25%) were hospitalized at least once for a life-threatening medical condition. On review of systems, individuals most commonly experienced neurologic (66, 71.7%) and gastrointestinal (53, 57%) symptoms. The most common specific conditions were constipation [N= 33 (36%)], frequent ear infections [N=34 (37%)], seizures [N=43 (47%)] and sleep disorders [N= 42 (46%)]. The most prominent discrepancy between

living and deceased participants was the presence of seizures which occurred in 35 (43%) of living and 8 (80%) of deceased participants.

Conclusions: Our findings are consistent with previous reports in regards to high rates of elevated BMI, sleep disturbance, epilepsy, and constipation. Chronic medical conditions affecting the adult ASD population necessitate ongoing access to primary care and disease management. Further analyses are underway to examine the patterns of medication use and the clustering of common symptoms across medical conditions in this population.

148.003 Psychiatric Co-Morbidity Among Adults with Autism Spectrum Disorder. D. Bilder*¹, J. Viskochil², T. Buck¹, H. Coon¹, W. M. McMahon¹ and M. Farley¹, (1)University of Utah, (2)Utah Autism Research Program

Background: Understanding the presence of co-morbid psychiatric disorders has important implications for our understanding of adult outcomes and service needs for individuals with autism spectrum disorders (ASD). Several studies have found high rates of co-morbid psychiatric conditions among children and adolescents with ASD. Unfortunately, the frequencies of these conditions have not yet been established in a representative sample of adults. Studies of children and adolescents with autism have shown high rates of Axis I psychiatric co-morbidity, frequently involving more than one disorder. Results among adult studies have been variable, although most find that depression and anxiety are common, particularly in individuals with high functioning autism or Asperger's Disorder. Yet, some studies suggest that the higher incidence of co-morbid psychiatric disorders found in children with autism does not persist into adulthood. Thus, a comprehensive assessment of current functioning and important characteristics outside the realm of ASD diagnostic criteria is critical to our understanding of the natural course and ultimate outcome of adults with ASD. The Mini PAS-ADD Interview assesses Axis I psychiatric disorders. There is no one tool that has established validity, reliability, and cut-off scores for this use in adults with autism across the spectrum of intellectual ability. The Mini PAS-ADD is a reliable and valid tool for use in adults with intellectual disabilities (ID) and identifies seven subscales of Axis I co-morbidity based on the ICD-

10 diagnostic algorithms of the Schedules for Clinical Assessment in Neuropsychiatry (SCAN).

Objectives: This study examines adults with ASD to (1) determine the presence of co-morbid psychiatric disorders and (2) identify the patterns of psychiatric symptoms and disorders affecting this population-based adult ASD sample.

Methods: As part of a large adult outcomes study, individuals with ASD (and their caregivers) ascertained during a 1980's state-wide Utah autism epidemiological study participated in a semi-structured interview querying the current and lifetime presence of psychiatric symptoms. The Mini PAS-ADD Interview was administered to caregivers of 132 participants between the ages of 24 and 54 with either DSM III autism (N= 107) identified in the original study or DSM-IV-TR autism spectrum disorder (N= 25), identified during a reclassification study. We applied the established cut-off scores to determine case definition for each disorder.

Results: Of the 132 participants, 73 (55%) met the case definition for a current co-morbid psychiatric disorder and 92 (70%) for a lifetime co-morbid psychiatric disorder. The most frequently experienced co-occurring psychiatric disorder for both current and lifetime conditions was Anxiety Disorder, [N = 51 (39%) and 70 (53%), respectively]. Obsessive-Compulsive Disorder was also quite common, affecting 43 (33%) participants currently and 48 (36%) participants during their lifetime. Other co-occurring psychiatric disorders, current and lifetime respectively, were Depressive Disorder [1 (1%), 17 (13%)], Expansive Mood [2 (2%), 8 (6%)], and psychosis [6 (5%), 13 (10%)].

Conclusions: Co-morbid psychiatric disorders occur frequently in adults with ASD. Using standard criteria, adapted for individuals with intellectual disability, is an effective means of identifying psychiatric disorders in this population.

148.004 Effect of Urbanicity On Adult Outcomes in Autism Spectrum Disorders. J. Viskochil*¹, M. Farley², D. Bilder², W. M. McMahon², S. Harward², E. Haygeman² and A. V. Bakian², (1)Utah Autism Research Program, (2)University of Utah

Background: Distinctions based on urbanicity have become increasingly provocative in the field

of autism research. Multiple studies reveal differences in characterization and presentation of autism spectrum disorders between urban and rural geographies, including discrepancies in prevalence, age of diagnosis, severity of comorbid disorders, and the need for and access to healthcare services. These variations engender implications regarding etiology, assessment, and the provision of services; however, reliable relationships between these variables and the degree of urbanicity must be established. Understanding the nature of differences in autism between urban and rural cases is paramount in addressing the adequacy of healthcare related service delivery.

Objectives: To elucidate differences in health and social outcomes for adults with autism spectrum disorders based on urbanicity. Participants were described as urban or rural residents according to U.S. Census definitions.

Methods: This study used 30-year follow-up data from a population-based sample of 305 individuals. Urban and rural classifications were based on county of residence and the determination of county demographics by the U.S. 2010 Census. Outcome variables included demographic factors, education and employment history, activities of daily living, access to healthcare services, and medical and psychiatric comorbidity. Procedures included direct assessment of the participants and semi-structured interviews and checklists completed with caregivers or family members. An outcome coding schema of employment, relationships, independence and an overall composite of functioning was created based upon a thorough review of each case.

Results: Of the original sample, 58 cases were excluded due to mortality or invalid current addresses (29 and 29, respectively), reducing the sample to 247 individuals. Of this, the majority were male (77%) living in an urban county (86%). The average age of this sample was 37 (SD 5.9, range 28-55). Group differences for education and employment suggested higher levels of education in the urban sample but a high proportion of participants currently employed in the rural sample, although neither comparison was significant. There was a trend for those living in urban areas to have more relationships and

social interaction ($z=1.55$, $p=0.06$). No substantial differences were found for independence or overall composite of functioning. Use of services was higher in the urban sample for hospitalizations, case management, psychiatric services, nursing, and therapy; however, none of these reached significance. Conversely, respite care was significantly higher in the rural sample ($z=2.32$, $p<.01$). Caution should be used in interpreting this finding due to small sample size and high standard deviation. There were no differences based on urbanicity between psychiatric comorbidities, medical diagnoses, or use medication use.

Conclusions: Although there were several differences in participant outcomes based on urban and rural status, few reached statistical significance in this sample. The trend for those in urban settings to have more social interaction is reasonable given greater population density. From a practical standpoint, the trend for those in rural areas to have higher rates of current employment may suggest that there is greater job retention in rural areas for individuals with autism spectrum disorders.

149 The Insula and Anterior Cingulate Cortex: Salience, Interoception, and Autism Symptoms

Moderator: C. Cascio Vanderbilt University School of Medicine

Organizer: C. Cascio Vanderbilt University School of Medicine

Autism spectrum disorders (ASD) are defined by impairments in reciprocal social interaction, communication, and the presence of repetitive patterns of behavior. These symptoms are defined by a tendency to disengage from external sensory stimuli, with the exception of idiosyncratic stimuli (e.g. sensory interests, circumscribed interests) that may be engaged intensely and/or repetitively. This pattern suggests a possible alteration in the balance between the reward value of internal relative to external sensory inputs in ASD. The insula is known for its role in monitoring internal state, a sensory process known as interoception, and evaluating internal signals for affective significance using inputs from limbic structures. The insula and the anterior cingulate cortex constitute the salience network, which uses this information about affective significance to facilitate switching attention from internal (default mode) to external loci. The role of the insula and anterior cingulate in ASD has only recently begun to be explored. This series of presentations provides evidence from neuroimaging and behavioral approaches for differences in the salience network, including enhanced interoception, as well as altered structure and function of the salience network, in ASD and in association with autistic traits in the general population.

149.001 Atypical Morphometry in the Cingulate and Insula and Its Relation to Impaired Social Cognition in Children and Adults with Autism Spectrum Disorder. E. G. Duerden*¹, K. A. R. Doyle-Thomas², J. P. Lerch¹, M. J. Taylor³ and E. Anagnostou³, (1)*The Hospital for Sick Children*, (2)*Holland Bloorview Kids Rehabilitation Hospital*, (3)*University of Toronto*

Background:

Previous functional neuroimaging studies have reported differential activation in the cingulate and insula in relation to social impairments in individuals with ASD. However, as of late more recent morphometric studies have indicated that structural atypicalities in these brain regions may also contribute to impaired social abilities in this sample.

Objectives:

To explore structural abnormalities in the cingulate and insula in children and adults with ASD and how they relate to social cognitive deficits.

Methods:

First, a meta-analysis was performed on the data from 19 structural imaging studies examining grey matter density alterations in children and adults with ASD. Probabilistic maps of grey and white matter differences in the ASD populations relative to healthy controls were calculated using the Activation Likelihood Estimate (ALE) method.

Then, a total of 28 children and adults (age range: 7-39 years) who carried a clinical diagnosis of ASD underwent magnetic resonance imaging (MRI) at 3 Tesla. Cortical thickness and surface area were calculated using a standard protocol within the CIVET processing pipeline. Surface area values were calculated for the each cortical lobe, the parahippocampal gyrus, cingulate, insula and the isthmus of the cingulate gyrus.

Results:

Children were more likely than adults to have increased grey matter in the cingulate and insula. The results in our sample suggest that increased cortical thickness in the rostral portion of the anterior cingulate cortex is associated with greater

social impairments. Greater surface area in the insula and the isthmus of the cingulate gyrus was also associated with more severe social cognition deficits.

Conclusions:

Findings indicate that structural atypicalities in the cingulate and insula are associated with impaired social processing, with some evidence for developmental changes. Future work will focus on combined functional and structural studies to elucidate the neural mechanisms of social impairments in both children and adults with ASD.

149.002 Revealing Insula Functional Circuit(s) and Their Role in Autism with Resting State fMRI. A. Di Martino*¹, C. Kelly², F. X. Castellanos² and M. P. Milham³, (1)*NYU Child Study Center*, (2)*Institute for Pediatric Neuroscience*, (3)*Center for Developing Brain at Child Mind Institute*

Background:

Mounting evidence support the model that patterns of intrinsic functional connectivity (iFC) trace the history of evoked co-activation within distinct neuronal networks. This, along with its high test-retest reliability and feasibility for data collection in more challenging populations, have increasingly placed R-fMRI among the mainstream neuroimaging modalities –particularly to map differences in functional architecture for autism spectrum disorders (ASD). Motivated by our ability to dissect functional units of complex regions such as the anterior cingulate cortex (ACC; Margulies 200X), and the insula (Kelly, 2012), and given their aberrant activation in individuals with ASD (Di Martino et al, 2009), we hypothesize a role of their functional connections in ASD.

Objectives:

Leveraging on the increased recognition of the dimensional nature of autistic traits, we employed the Social Responsiveness Scale-Adult version (SRS-A) as a first step to identify a brain behavioral relationship potentially useful for ASD.

Methods:

Resting state fMRI scans were collected in 25 neurotypical individuals (26.4 ± 5.6 y) who

provided SRS-A completed by an informant who knew the participant in natural social settings. We selected the pregenual ACC (pgACC), typically implicated in theory of mind processes, as a region of interest and mapped its whole brain iFC with and without the SRS-A as a covariate of interest. Voxel-wise analyses were Gaussian random field corrected for multiple comparisons at $Z > 2.3$; $p < .05$. The study has been approved by the IRB of the NYU school of medicine and the NYU.

Results:

We found a significant negative relationship between SRS-A and pgACC iFC with the anterior portion of mid-insula. Specifically, low levels of autistic traits were observed when a substantial portion of the anterior mid-insula showed positive iFC with pgACC - an iFC pattern similar to the ventral anterior insula typically implicated in empathy processes. In contrast, elevated levels of autistic traits were associated with negative iFC between the pgACC and the anterior mid-insula.

Conclusions: Intrinsic FC of the pgACC-insula is dimensionally related autistic traits in neurotypical adults. Application of this approach in individuals with ASD is needed to confirm whether the pgACC- anterior mid insula circuit is a marker of ASD risk. Additionally, given the role of other portions of insula and ACC in cognitive and sensory processes we planned a broader examination of their functional connections in individuals with ASD.

149.003 Superior Interoception in Children with Autism Spectrum Disorders. C. Cascio*¹, W. A. Loring² and K. Schauder¹,
(1)Vanderbilt University School of Medicine, (2)Vanderbilt University

Background:

Although differences in processing external sensory inputs are widely reported and increasingly studied in ASD, little is known about the ability of children with ASD to attend to and perceive sensory signals from within their own bodies. The insula is important for perception of bodily signals and has been implicated in empathy as well as affect-based direction of attention as part of the salience network, both of which have relevance for ASD. Although interoception is

linked with empathy and thus may be predicted to be impaired in ASD, our hypothesis was that children with ASD would show enhanced interoception. This prediction was based on a model positing that internal sensory cues may compete with external cues for salience in ASD.

Objectives:

To measure interoceptive ability in a group of children with ASD, compared to a matched group of children with typical development.

Methods:

10 children with ASD and 15 typically developing children (ages 8-17) were monitored for heart rate using a pulse oximeter over four intervals: 25, 35, 45, and 100 seconds. Participants were asked to focus on their heartbeat and count the number of heartbeats during each interval. An error rate was calculated as the absolute value of the difference between perceived and actual heartbeats, expressed as a percentage of the actual number of heartbeats. Effects of group and interval were assessed with a repeated measures ANOVA.

Results:

There was a significant group*interval interaction, which follow-up tests indicated was driven by significantly better performance by the ASD group at the longest interval. There was a trend for a main effect of group, with the ASD group performing better overall (lower error rate) on the task.

Conclusions:

We found interoceptive ability to be enhanced in a sample of children with ASD, particularly over a long time interval for which typically developing children performed most poorly. This may point to heightened salience of internal sensory cues, which is consistent with sensorimotor studies suggesting aberrant reliance on proprioceptive relative to visual cues. Future work will investigate the role of the insula in enhanced interoception in ASD.

149.004 Saliency Network Based Classification and Prediction of Symptom Severity in Children with Autism. L. Uddin*, K. Supekar, C. Lynch, A. Khouzam, J. M. Phillips, C. Feinstein, S. Ryali and V. Menon, *Stanford University*

Background:

Autism spectrum disorders (ASD) affect 1 in 88 children and are characterized by a complex phenotype including social, communicative, and sensorimotor deficits. ASD has been linked with atypical connectivity across multiple brain systems, yet the nature of these differences in young children with the disorder is not well understood.

Objectives:

We examined connectivity of large-scale brain networks and determined whether specific networks could distinguish children with ASD from typically developing (TD) children and predict symptom severity in children with ASD.

Methods:

We utilized a case-control design using functional magnetic resonance imaging. Twenty 7-12 year-old children with ASD and twenty age-, gender-, and IQ-matched TD children participated in the study. Our main outcome measures were: (1) Between-group differences in intrinsic functional connectivity of large-scale brain networks, (2) performance of a classifier built to discriminate children with ASD from TD children based on specific brain networks, and (3) correlations between brain networks and core symptoms of ASD.

Results: We observed stronger functional connectivity within several large-scale brain networks in children with ASD compared with TD children. This *hyper*-connectivity in ASD encompassed salience, default mode, fronto-temporal, motor, and visual networks. No large-scale networks showed stronger connectivity in TD children compared with children with ASD. This *hyper*-connectivity result was replicated in an independent cohort obtained from publicly available databases. Using maps of each individual's salience network, children with ASD could be discriminated from TD children with a classification accuracy of 78% ($p < 0.03$), 75%

sensitivity and 80% specificity. The salience network, comprised of anterior cingulate and anterior insular cortices, showed the highest classification accuracy among all networks examined, and BOLD signal in this network predicted restricted and repetitive behaviors.

Conclusions:

Saliency network *hyper*-connectivity may be a distinguishing feature in children with ASD. Quantification of brain network connectivity is a step towards the development of biomarkers for objectively identifying children with the disorder.

150 Genomic and Systems Biological Approaches to Understanding Autism Spectrum Disorder

Moderator: M. W. State *Yale University School of Medicine*

Organizer: A. J. Willsey *Yale University School of Medicine*

Recent gene discovery efforts focusing on *de novo* variation have rapidly expanded the number of genes and loci reliably associated with ASD. However, locus heterogeneity and biological pleiotropy have complicated the effort to clarify the neurobiology of ASD. Still, multiple lines of evidence suggest that the large number of risk genes will converge on a smaller number of pathophysiological mechanisms. Importantly, emerging maps of gene expression in the developing brain and the ability to generate similar datasets for gene regulatory interactions provide a powerful and novel means to identify points of mechanistic convergence for novel ASD genes within a developmentally-relevant framework. The proposed panel will describe an ongoing multi-disciplinary collaboration aimed at clarifying molecular and circuit level pathology in ASD. Included are presentations on: 1) New data from ongoing whole-exome sequencing studies of the Simons Simplex Collection; 2) expression analyses of ASD loci in the developing brain; 3) ChIP-seq studies of ASD genes involved in epigenetic regulation; and 4) a paradigm for integrating these data to clarify ASD pathology. This collaborative approach offers a path forward from unbiased gene discovery to the illumination of convergent molecular mechanisms underlying ASD.

150.001 ASD Gene Discovery with Whole-Exome Sequencing. S. J. Sanders*¹, A. J. Willsey¹, S. Dong¹, B. Devlin², K. Roeder³, N. Sestan¹, J. P. Noonan¹ and M. W. State¹, (1)*Yale University School of Medicine*, (2)*University of Pittsburgh*, (3)*Carnegie Mellon University*

Background: ASD is a highly heritable disorder, however ASD gene discovery has been hindered by the extensive locus heterogeneity. *De novo* copy number variation (CNVs) and *de novo* loss of function (LoF, i.e. nonsense, canonical splice site and frameshift) variants have been associated with ASD through the observation of a higher rate of such variants in cases than unaffected controls.

Objectives: To identify ASD-associated genes through whole-exome sequencing; to use these genes to inform on the underlying etiology of ASD.

Methods: We present the analysis of 300 new ASD families from the Simons Simplex Collection analyzed with whole-exome sequencing as well as a combined re-calling and re-analysis of previously published ASD exome data from 965 families, yielding a total of 1,265 families. The analysis focuses on multiple *de novo* mutations clustering in the same gene in unrelated probands. Statistical thresholds for genome wide significance were established using previously described methods, taking into account the type of mutation (LOF vs missense etc), the sequence context including GC content, and gene size.

Results: This study is ongoing: at the time of submission a total of 147 genes were observed to have at least one *de novo* LoF variant in an affected individual. Based on the distribution of *de novo* LoF variants in the unaffected siblings, 60% of these genes are expected to be associated with ASD. Five of these 147 genes had two *de novo* LOF mutations ($p=0.04$ and $q=0.006$) and four showed three independent LoF variants ($p=0.0001$, $q=0.0002$). Furthermore, this observation of nine ASD-associated genes with at least two hits, and the time course with which they were identified, is consistent with a model of 1,000 genes contributing to ASD causation. A further four genes were identified as being highly likely to contribute to ASD causation based on the additional information derived from inherited LoF and *de novo* 'probably damaging' missense variants. Analysis of the 147 *de novo* LoF variants with the DAVID functional annotation tool yielded a single biological process that survived correction for multiple comparisons: chromatin organization ($p=0.04$).

Conclusions: Whole-exome sequencing provides a means to reliably identify genes that carry large risks for ASD. Analysis of the 147 *de novo* LoF variants with the DAVID functional annotation tool yields a single, statistically significant biological process, chromatin organization, implying that direct analysis of gene regulatory and expression networks could provide important new insights into the pathophysiology of ASD. While this study supports prior estimates of extensive locus

heterogeneity, functional enrichment results comport with prior data suggesting that these genes will likely converge on a much smaller number of relevant molecular mechanisms.

150.002 Identifying Targets of ASD-Associated Chromatin Regulators in the Developing Human Brain. R. A. Muhle¹, S. Reilly¹, W. Niu¹, S. J. Sanders¹, K. Roeder², B. Devlin³, M. W. State¹, N. Sestan¹ and J. P. Noonan^{*1}, (1)Yale University School of Medicine, (2)Carnegie Mellon University, (3)University of Pittsburgh

Background: Chromatin regulators have been identified among genes found to be associated with ASD via whole exome sequencing. These proteins alter covalent histone modifications or reposition nucleosomes to establish active and repressed chromatin states that enable tissue-specific gene expression. Chromatin regulators are thus essential for cell fate determination, developmental patterning, and the maintenance of cellular identity. Haploinsufficiency of these genes may contribute to ASD by disrupting gene expression in the developing brain, thereby compromising neuronal specification, neural circuit formation, arealization or other processes.

Objectives: We are investigating the role of multiple chromatin regulators in ASD using an unbiased experimental strategy that includes: a) Chromatin immunoprecipitation followed by high throughput sequencing (ChIP-seq) to map binding sites of ASD-associated chromatin regulators; and b) cross-referencing these binding data with genome-wide histone modification maps to identify target genes activated or repressed by specific chromatin regulators.

Methods: To validate our approach, we have used ChIP-seq to map binding sites for multiple genes carrying one or more *de novo* mutations based on four recently published whole exome sequencing studies. We simultaneously generated maps of histone modifications associated with active promoters and enhancers. Combining these data we will identify regulatory elements and their target genes under the control of ASD related chromatin modifying genes, thus revealing specific gene regulation mechanisms potentially affected by ASD-associated mutations.

Results: We show that histone modification maps and chromatin regulator binding data can be combined to identify regulatory elements and

associated genes putatively under the control of ASD-associated chromatin regulators. We will present specific data on genes implicated in ASD via recent whole exome sequencing data.

Conclusions: Our results demonstrate the feasibility of directly identifying the gene targets of ASD-associated chromatin regulators during brain development using ChIP-seq. Integrating these target datasets with maps of chromatin state and gene expression will allow us to define regulatory networks perturbed in ASD. This will provide insight into the developmental etiology of ASD and serve as a foundation for future experimental studies.

150.003 Developmental and Functional Analyses of Neural Circuits Affected in Autism Spectrum Disorders. M. Li¹, A. J. Willsey¹, S. J. Sanders¹, K. Kwan¹, C. Bichsel¹, A. Tebbenkamp¹, K. Roeder², B. Devlin³, J. P. Noonan¹, M. W. State¹ and N. Sestan^{*1}, (1)*Yale University School of Medicine*, (2)*Carnegie Mellon University*, (3)*University of Pittsburgh*

Background: ASD are a spectrum of disorders likely resulting from aberrant development and function of neural circuits. Copy number variation analyses and whole-exome sequencing have identified multiple novel ASD genes and loci, while at the same highlighting extensive genetic heterogeneity. This complexity and the biological pleiotropy of known risk genes has complicated the identification of specific cell types and circuits underlying ASD pathogenesis. Combined analysis of complementary expression and regulatory networks in the developing brain promises to provide new insights and testable hypothesis about what cell types are involved, as well as where and when developmental perturbations occur in the brain. However, methods to rigorously test these predictions and translate them to an actionable understanding of neurobiology in ASD are needed.

Objectives: To determine how genes associated with ASD shape the development and evolution of neuronal circuits of the human cerebral cortex.

Methods: Informed by spatiotemporal maps of gene expression, gene-regulatory interactions, and chromatin states, we have used traditional molecular biological and genetics tools to analyze the function and expression of ASD risk genes in the developing brain.

Results: Expression patterns of the diverse ASD risk genes in the developing brain provide novel insights into the underlying biology. One such example is the expression of the *FMR1* gene, which encodes an RNA-binding protein (FMRP) altered in Fragile X syndrome. We show that FMRP regulates translation of neuronal nitric oxide synthase 1 (NOS1) in the developing human neocortex. Whereas NOS1 mRNA is widely expressed, NOS1 protein is transiently co-expressed with FMRP during early synaptogenesis in layer- and region-specific pyramidal neurons. These include mid-fetal layer 5 subcortically projecting neurons arranged into alternating columns in the prospective Broca's area and orofacial motor cortex. Human NOS1 translation is activated by FMRP via interactions with coding region-binding motifs absent from mouse *Nos1* mRNA, which is expressed in mouse pyramidal neurons, but not efficiently translated. Correspondingly, neocortical NOS1 protein levels are severely reduced in developing human FXS cases, but not FMRP-deficient mice.

Conclusions: Our findings provide insights into cells and neural circuits affected in ASD and identify novel species-specific molecular mechanism altered in the leading monogenic cause of intellectual disability and autism, FXS. Importantly, this study illustrates a process of moving from genetic findings, to expression analysis, to functional characterization in order to expand the understanding of human-specific molecular mechanisms that may be compromised in ASD.

150.004 Finding Convergent Biology with Expression Analysis of ASD Risk Genes. A. J. Willsey^{*1}, M. Li¹, S. J. Sanders¹, J. Gockley¹, Z. Lin¹, Y. Zhu¹, B. Devlin², K. Roeder³, J. P. Noonan¹, N. Sestan¹ and M. W. State¹, (1)*Yale University School of Medicine*, (2)*University of Pittsburgh*, (3)*Carnegie Mellon University*

Background: Recent advances in genomics and transcriptomics are providing unprecedented opportunities to dissect the molecular mechanisms underlying ASD. On the one hand, a series of recent studies have demonstrated that *de novo* mutation discovery via whole exome sequencing and copy number variation analyses provide a systematic unbiased approach to gene discovery. At the same time, the availability for the first time of a detailed map of gene expression in normal brain is offering the ability to search for points of

spatial and temporal convergence among the disparate set of genes clearly identified as carrying ASD risk. Given the high degree of genetic heterogeneity underlying ASD, the combination of reliable gene discovery and expression profiling offers the potential to identify convergent biological processes and reveal novel treatment targets.

Objectives: To leverage spatiotemporal gene expression data to build expression networks in a developmentally-relevant framework in order to converge ASD risk genes into functional pathways underlying ASD neurobiology.

Methods: Gene expression networks were constructed using spatiotemporal gene expression data in the developing brain.

Results: Gene expression networks containing ASD risk genes are dynamic across development. Clusters generated from correlation analyses of gene expression in the neocortex highlight the importance of early and mid-fetal development at a time when early synaptic connections are being formed in these regions.

Conclusions: Spatiotemporal brain expression analysis makes meaningful and testable predictions about ASD biology. As the number of risk genes increases, we expect far greater resolution to detect the biological processes, brain regions, and developmental periods fundamental to ASD neuropathology.

151 Beyond the RCT: Extending Delivery of the Early Start Denver Model in the Real World to Foster Best Practice

Moderator: C. Dissanayake La Trobe University

Organizer: C. Dissanayake Olga Tennison Autism Research Centre

The Early Start Denver Model (ESDM; Rogers & Dawson, 2010) is a manualized, developmentally oriented play-based intervention incorporating principles of Applied Behaviour Analysis, Pivotal Response Training and relationship-based methods. Designed for infants, toddlers and preschoolers with ASD, the crucial components include use of an interdisciplinary team to address a range of challenges including a focus on the child's affect, attention and arousal in the teaching procedures. The efficacy of the ESDM has been documented in a randomized clinic controlled study (Dawson, Rogers, et al., 2010), in which participants aged between 18- to 30-months received an average of 15 hours a week of 1:1 ESDM intervention by trained therapists. Significant improvements were found in the ESDM group compared to the 'treatment-as-usual'

community group, across a variety of developmental domains at the 2-year follow-up. The suite of papers in this symposium, from across the world, present findings from the next steps in development of the ESDM: extension of the ESDM to group-based delivery in a community-based setting (1) and the development of experimental measures to predict treatment outcomes in group-based delivery (2; Australia), examination of social reward on learning (3; USA) and translation of the ESDM into an Italian context (4; Italy).

151.001 Group Delivery of the Early Start Denver Model: Treatment Outcomes. C. Dissanayake*¹, C. D. Zierhut² and G. Vivanti¹, (1)*La Trobe University*, (2)*UC Davis MIND Institute*

Background:

Research on the ESDM has been conducted with 1:1 in-home delivery of moderate intensity (e.g., 15 - 20 hours per week consistent with recommendations for intervention for children with autism (National Research Council, 2001). The Margot Prior Wing Autism Specific Early Learning and Care Centre (MP Wing ASELCC) is one of only two sites worldwide currently implementing the ESDM in a group setting. This is the first study to examine the translation of the ESDM into community practice by investigating developmental change in children receiving the ESDM in a group setting.

Objectives:

The first aim was to examine treatment progress for children who have received a moderate level of intensity of group-based ESDM for a period of at least one year. The second aim is to examine the predictors (i.e., cognitive ability, autism severity) of treatment progress after one year of group delivery of ESDM.

Methods:

Participants comprised 25 toddlers and preschool aged children diagnosed with an ASD aged between 2- to 5-years. Autism diagnoses were confirmed with the Social Communication Questionnaire and the Autism Diagnostic Observation Schedule (ADOS; 20 met criteria for AD, and 5 met criteria for ASD), and cognitive ability was assessed using the Mullen Scales of Early Learning (MSEL). All children were also administered the ESDM Curriculum Checklist which is a developmentally sequenced tool utilized to assess all developmental areas, and which guides learning objectives on a quarterly basis.

These measures were readministered after one year of treatment, and outcomes at one year post treatment was ascertained via change scores on each of these measures.

Results:

Children showed significant treatment gains over the course of the year as evidenced by performance on all domains of the ESDM Curriculum Checklist, and all subscales of the MSEL, with the exception of the fine motor subscale, relative to baseline scores. The best predictors of treatment gains were symptom severity, cognitive level and receptive language abilities at baseline. Chronological age at baseline was not a predictor of treatment gains, suggesting that preschoolers might benefit from the treatment even if commenced after 36 months of age.

Conclusions:

The findings suggest that children receiving ESDM in a group setting make considerable treatment gains with appropriate levels of intensity. This model, with its focus on very young children, is ideally suited for implementation within early learning settings such as childcare. Establishing the effectiveness of the ESDM in group settings represents an important endeavour, to underpin wider access to this evidence-based model of EIBI.

151.002 Social and Non-Social Abilities Are Differentially Associated to Treatment Gains in Different Domains. G. Vivanti*¹, C. D. Zierhut² and C. Dissanayake¹, (1)*La Trobe University*, (2)*UC Davis MIND Institute*

Background: Early intensive behavioural interventions such as the Early Start Denver Model have been shown to improve social and communicative outcomes in autism. However, children with autism display individual differences in response to treatment. Understanding the predictors of differential outcomes is crucial for enabling practitioners to prospectively recommend treatment strategies for specific children in order to increase the overall rate of positive outcomes.

Objectives: Our aim was to identify the individual differences in early emerging social and cognitive abilities which are associated with differential

responses to treatment. To allow for a fine-grained measurement of such abilities we used four novel experimental paradigms.

Methods: The experimental tasks assessing early emerging social and non-social cognitive abilities were administered to the 25 children with an ASD enrolled in the MP Wing ASELCC program aged 2- to 5-years. The Functional Use of Objects task assessed participants' ability to engage in purposeful (versus purposeless) actions on objects. The Social Understanding task assessed the ability to anticipate others' goals on an eye-tracking task. The Social Attention measure assessed the amount of attention to social versus non-social stimuli in the same eye-tracking paradigm. Finally a behavioural task assessed imitation abilities.

Given the importance of these early emerging abilities for social learning, we tested the hypothesis that children who show more advanced skills in the four specified areas will derive the most benefit from the ESDM program in terms of developmental and behavioural gains.

Results: Our analyses show that functional use of objects and imitation predicted gains in nonverbal DQ ($r=.8$ and $.7$ respectively; $p<.005$), whilst social understanding was a significant predictor of verbal DQ ($r=.5$; $p<.05$). Surprisingly, individual differences in social interest were not associated with developmental gains.

Conclusions: Individual differences in early emerging social and non-social cognitive abilities were differentially associated to gains in different developmental areas. These preliminary data suggest that the ESDM might be particularly beneficial to children whose cognition is more "organized" around goals, as reflected in the use of objects in a goal-directed way, the understanding of goals behind others' actions and the imitation of others' goal-directed actions. The introduction of theory-driven experimental tasks in treatment studies might allow for a more fine-grained analysis of social-cognitive and learning profiles associated to differential treatment outcomes.

:

151.003 Assessing the Effect of Reward On Learning: A Novel Eye-Tracking Marker of Treatment Outcome. C. McCormick^{*1}, G. S. Young¹ and S. J. Rogers², (1)*UC Davis MIND Institute*, (2)*MIND Institute; University of California at Davis*

Background : Autism symptoms may develop in part due to diminished salience of social stimuli (Dawson et al., 2004; Dawson, Webb, & McPartland, 2005; Mundy, 2003). Many intervention programs, including the Early Start Denver Model (ESDM), focus on social motivation and social engagement, with the goal of changing the reward value of social stimuli.

Objectives : The goal of this study was to develop an eye-tracking task sensitive to the effects of social and non-social reward on learning that could discriminate differences in early ASD and typical development.

Methods : To date, 17 children with typical development (TD; 12 male; mean age 48.71 (4.04) months) and 16 children with ASD (13 male; mean age 49.44 (4.37) months) have completed the protocol. All children with ASD had received a diagnosis at two years, prior to the study, and intensive behavioural intervention. In the paradigm, children were rewarded with an interesting video (social or non-social) when they fixated on the same target location located in a circular array of six identical blue dots. Learning criterion was defined as first fixation to the target for three trials out of six within a block, after which a new block of trials began with a new target location and reward. Learning was measured by number of trials per block, where fewer trials indicate better performance. Thus, participants had to learn the overall paradigm, as well as the new location for each block.

Results : Multilevel models were fit using the MIXED and NL MIXED procedure in SAS (Littell, Miliken, Stout, & Wolfinger, 1996) with maximum likelihood estimation method and number of trials per block as the dependent measure. Four models were tested: no growth, linear, quadratic and exponential growth. The best fit was the quadratic model. There was a significant negative linear slope ($\beta = -0.22$, $t(32) = -2.86$, $p = .01$) and a positive quadratic slope ($\beta = 0.01$, $t(32) = 2.04$, $p = .05$). Overall, the ASD group had a higher intercept than the TD group ($\beta = 0.66$, $t(280) = 3.16$, $p < .01$); indicating poorer performance. There was also a significant negative effect of

social reward on the intercept ($\beta = -0.41$, $t(279) = -3.29$, $p = .001$). There was no interaction between group and reward type or group and linear or quadratic slope; however there was a significant interaction between the linear slope and reward condition ($\beta = -0.11$, $t(278) = -3.08$, $p < .01$) indicating that on trials with a social reward, both groups demonstrated faster learning. Final analyses will divide the ASD group into ESDM intervention and community intervention to assess treatment related differences. We predict the ESDM group will be more sensitive to social rewards than the community intervention group due to the emphasis on social engagement in the ESDM.

Conclusions : Children with ASD did not perform as well as the TD children; however, they demonstrated the same pattern of learning. The ASD group showed enhanced social versus non-social reward value. This study demonstrates the feasibility of using gaze contingent eye tracking protocols with young children with and without disability to examine social reward salience as a treatment outcome.

151.004 The Early Start Denver Model in Italy. C. Colombi^{*1}, F. Muratori², G. Pioggia³, A. Narzisi², L. Ruta⁴, R. Siracusano⁵ and G. Tortorella⁵, (1)*National Research Council of Italy*, (2)*University of Pisa – Stella Maris Scientific Institute*, (3)*Institute of Clinical Physiology, National Research Council (CNR)*, (4)*University of Cambridge*, (5)*Universita' di Messina*

Background: Research on the ESDM has been conducted mainly in the United States and exclusively in English speaking countries. To our knowledge, the Prima Pietra Project based at the Pervasive Healthcare Center of the Institute of Clinical Physiology of the National Research Council of Italy (Consiglio Nazionale delle Ricerche, C.N.R.) and of the AOU Polyclinic "G. Martino" in Messina is the first study investigating ESDM within an Italian speaking population. Just recently, very young children have begun to be diagnosed with ASDs in Italy through early screening and identification campaigns, also supported by early risk assessment web-based platforms. As children receive early diagnoses, it is necessary to develop best practices for early intervention.

Objectives: The first aim was to evaluate whether the ESDM could be disseminated to Italian professionals. The second aim was to

examine the progress of the children enrolled in the study.

Methods: Participants comprised 10 toddlers and preschoolers diagnosed with an ASD aged between 24- to 44 months. Autism diagnoses were confirmed with the Autism Diagnostic Observation Schedule, and cognitive abilities were assessed using the Griffiths Developmental Quotient. Children participated in the "Learning ESDM" treatment, an ESDM based intervention in which therapists were learning the model. Children received between 5 to 10 hrs of treatment per week for 6 months and were assessed at entry, after 3 months, and at the end of the intervention.

Results: Preliminary results show that children are making progress as demonstrated by gains on the ESDM Curriculum Checklist and on the Griffiths Developmental Quotient. Therapists are learning the model as demonstrated by improvements on the ESDM fidelity measure.

Conclusions: Our preliminary results suggest that it is possible to learn and deliver the ESDM intervention in an Italian research centre. Children's progress provides support for the ESDM as an effective early intervention model. Establishing the feasibility and the effectiveness of the ESDM in our study represents an important step toward wider access to this evidence-based model outside the United States.

Keynote Address Program

152 The Epidemiology of Autism Spectrum Disorder: Toward a More Inclusive World

We live in an era of exciting advances in our awareness and understanding of autism spectrum disorder, but also a time of enormous global imbalance. Most of what is known about the epidemiology, genetics, clinical manifestation and course, treatment, and nearly every other aspect of autism is based on research in high income countries, where fewer than 10% of births occur and less than 20% of the population lives globally. This talk will describe opportunities to expand the horizons of autism epidemiology and service delivery to include the 80 to 90% of affected individuals and families who live in low and middle income countries, as well as those who are socioeconomically disadvantaged and living in high income countries. It will also describe some of the cultural and financial barriers to progress, and make a case for incorporating concepts of the World Health Organization's International Classification of Disability and Functioning into the classification and epidemiology of autism

spectrum disorder, with the ultimate goals to include not only primary prevention of autism but also enhancement of participation and social inclusion of people with autism spectrum disorder.

152.001 The Epidemiology of Autism Spectrum Disorder: Toward a More Inclusive World. M. Durkin*, *University of Wisconsin-Madison*

153 Reversing Autistic Symptoms From Mouse to Man
Moderator: T. Hensch *Harvard University*

Organizer: T. K. Hensch *Harvard University*

The therapeutic promise of reversibility drives much of the research into mechanisms of autism spectrum disorders (ASD). This workshop will summarize recent advances in the ability to control critical periods of brain development and the successful recovery of function by various treatments in animal models of ASD. The concepts of excitatory-inhibitory balance, regulation of protein synthesis, and microglial activation will be highlighted. Plasticity at the right time and place is central to brain development and function throughout life. Sensory systems have revealed that cortical critical periods are driven by the dynamics of excitatory-inhibitory (E-I) circuit balance, which is often impaired in ASD. Circuit rewiring is a physical process, involving the pruning and construction of new connections, requiring well-orchestrated protein synthesis. Ultimately, molecular 'brakes' are expressed which actively clamp down on plasticity beyond early development. Resetting E-I balance or lifting these brakes in adulthood allows the successful reactivation of critical period plasticity. Correcting E-I imbalance with pharmacological inhibitors of neurotransmission is one way to rescue Rett syndrome in mice. Signaling cascades, including the mTOR pathway, couple neurotransmitter and neurotrophin receptors to the translation regulatory machinery during the formation of long-lasting synaptic plasticity. Mutations in the negative regulators of this machinery, such as Fragile X or eIF4E, are associated with ASD. Curbing the excessive protein synthesis may reverse these disorders. A further novel target may also include microglia, which normally contribute to synaptic pruning. Wild-type bone marrow transplants arrest disease pathology and increases life expectancy in Rett syndrome models, indicating an important role for immune-glia interactions as well. This session will consider the various rescue paradigms from the biological context of normal critical periods of brain development, which may be mis-timed or mis-regulated in ASD.

153.001 Reactivating Critical Periods of Brain Development. T. Hensch*, *Harvard University*

Background: Neural circuits are shaped by genes and environment during early windows of brain development. Recent work with classic models of deprivation amblyopia in animals has begun to unravel the cellular and molecular constraints that establish such 'critical' or 'sensitive' periods for plasticity. Of particular clinical relevance is the extent to which a critical period can be safely and non-invasively recapitulated.

Objectives: This talk will summarize mechanistic insight into the opening, execution and closure of circuit rewiring in the neocortex of mice. The aim is to establish key principles across systems and their relevance to autism spectrum disorders.

Methods: We focused on the pivotal role for late developing excitatory-inhibitory (E/I) circuit balance in the initiation of critical periods. Genetic disruption of GABA synthesis or the maturational state of parvalbumin (PV)-positive basket cells delays onset, while benzodiazepines or treatments that accelerate PV-circuit maturation trigger premature plasticity. Once induced, synaptic rewiring in response to monocular deprivation or tone-rearing is manifest by increased dendritic spine motility and pruning followed by regrowth. Moreover, inputs onto inhibitory PV-cells exhibit a dynamic bidirectional plasticity. These changes are ultimately hard-wired as part of the large-scale connectivity of afferent axons by the end of the critical period.

Results: Plasticity gradually winds down as a consequence of late-appearing molecular factors with a characteristic duration proportional to species' lifespan. Effects of early visual experience or deprivation are thus actively maintained throughout life. Two such classes of molecular "brakes" on plasticity have been identified: those that limit structural change and those that regulate E/I balance. Axonal growth inhibitors include myelin related proteins (NgR, PirB) or chondroitin sulphate proteoglycans forming tight peri-neuronal nets (PNNs) around mature PV-basket cells. Regulators of E/I balance include neuromodulators, such as serotonin and acetylcholine. Manipulation of any of these "brakes" enables the reactivation of visual cortical plasticity and recovery from amblyopia in adulthood.

Conclusions: The biology of the brain is heavily invested in the optimal timing and duration of plasticity, having evolved numerous molecular checks and balances. Notably, many of these cellular players are associated with critical period profile across systems, and may go awry in the etiology of developmental disorders, such as autism.

Background: Rett syndrome (RTT) is a complex autism spectrum disorder (ASD) caused by loss-of-function mutations in the gene encoding methyl-CpG-binding protein 2 (MeCP2), a transcriptional regulatory protein. RTT patients suffer from severe impairments in cognition, motor control, respiration and autonomic regulation, and many exhibit autistic behaviors. Altered functional connectivity has been identified in some brain regions in mouse models of RTT and other ASDs and in imaging studies of individuals with autism. However, a map of circuit dysfunction in the RTT brain as a whole has been lacking, hampering our ability to understand the complexity of neurologic dysfunction in this disorder and identify therapeutic targets. Mapping global network dysfunction is especially important in understanding RTT because prominent features of the disease, such as abnormal cardiorespiratory control, are highly dependent on behavioral state, suggesting that interactions between distant structures, such as the forebrain and brainstem, are abnormal.

Objectives: 1) To map regional differences in brain activity between *Mecp2* mutant and wildtype (Wt) mice with high anatomic resolution, and 2) Determine whether or not circuit dysfunction in *Mecp2* mutants is reversible by treatment with small molecule therapeutic agents *in vivo*.

Methods: Neural circuit function in *Mecp2* mutant (*Mecp2^{tm1.1Jae/y}* and *Mecp2^{tm1.1Jae/+}*, *129/B16/BalbC*) and Wt mice was mapped *in situ* using immunochemical localization of the activity-dependent, immediate early gene product Fos, combined with whole-cell patch clamp recording from isolated brain slices *in vitro*. Prepulse inhibition of acoustic startle (PPI), an index of sensorimotor gating, was used as a behavioral outcome measure. Animals were randomly assigned to treatment groups and observers were blinded to genotype and treatment.

Results: Fos mapping revealed significant differences in brain activity across the neuraxis between *Mecp2* mutants and Wt mice. Specifically, we identified a large domain, rostral to the pons, in which RTT mice exhibit significantly lower activity than Wt, including key nodes in the default mode network (DMN; medial

prefrontal, cingulate and retrosplenial cortices) as well as sensory and motor cortices. Forebrain hypoactivity in mutants was associated with markedly exaggerated PPI responses compared to Wt. In contrast, medullary regions important for cardiorespiratory homeostasis exhibited higher activity than Wt, including increased frequency of spontaneous excitatory postsynaptic currents (EPSC) and increased evoked EPSC amplitudes. Acute treatment of mutant mice with the NMDA receptor antagonist ketamine restored wildtype levels of Fos expression in the forebrain and completely reversed deficits in PPI, even at sub-psychotomimetic doses (8 mg/kg, i.p.).

Conclusions: Neurological abnormalities in *Mecp2* mutant mice are associated with excitatory/inhibitory imbalance across the forebrain-midbrain-hindbrain axis, including hypoactivity in the forebrain default mode network and hyperactivity in the caudal brainstem. In light of recent findings that the default mode network is also hypofunctional in autism, our data raise the possibility that reduced activity within this meta-circuit is a shared feature of RTT and other ASDs and is reversible by treatments targeting ketamine-sensitive signaling pathways. On the other hand, hyperactivity within the caudal brainstem may underlie the disturbances in respiratory and autonomic control that generally distinguish RTT from other disorders within the autism spectrum.

153.003 Reversing Synaptic Dysfunction and Aberrant Behavior in Mouse Models of Autism Spectrum Disorder. E. Klann*, *New York University*

Background: A requirement for de novo protein synthesis is one of the hallmarks of long-lasting synaptic plasticity and long-term memory. An increasing number of studies, including several from our laboratory, have identified signaling cascades, including the mTORC1 signaling pathway, that couple neurotransmitter and neurotrophin receptors to the translation regulatory machinery during the formation of long-lasting synaptic plasticity and the consolidation of long-term memory. Interestingly, mutations in negative upstream regulators and downstream effectors of mTORC1, including fragile X mental retardation protein (FMRP) and the eukaryotic initiation factor 4E (eIF4E) are associated with several types of developmental disability and autism spectrum disorder (ASD).

Objectives: Our objective is to determine whether exaggerated protein synthesis is a causative factor for synaptic dysfunction and aberrant behavior in mouse models of ASD, including fragile X syndrome (FXS) model mice and transgenic mice that overexpress eIF4E.

Methods: FXS model mice and eIF4E transgenic (eIF4E Tg) mice were examined for exaggerated protein synthesis and altered translational control. First, we identified the altered translational control mechanisms in the brains of FXS and eIF4E Tg mice. Then we utilized genetic and pharmacological approaches to target the translational control molecules of interest, including eukaryotic initiation factor 4F (eIF4F) and p70 S6 kinase 1 (S6K1).

Results: We found that genetic reduction of S6K1 in FXS model mice corrected exaggerated protein synthesis, abnormal synaptic plasticity, and multiple aberrant behaviors. We currently are determining whether treating FXS model mice with an inhibitor of S6K1 can reverse the aforementioned phenotypes. In addition, we have found that compounds that target eIF4F can reverse exaggerated protein synthesis and synaptic dysfunction in eIF4E Tg mice. Moreover, the eIF4F inhibitors reverse ASD-associated behaviors displayed by eIF4E Tg mice, including repetitive behaviors, behavioral inflexibility, and abnormal social behavior. We currently are determining whether the compounds that target eIF4F have similar effects on aberrant behaviors displayed by FXS model mice.

Conclusions: Our studies strongly suggest that exaggerated protein synthesis in mice triggers synaptic dysfunction and aberrant behaviors that are associated with ASD. These studies have revealed important links between abnormal translational control and synaptic dysfunction, as well as behaviors associated with ASD. Finally, these studies have provided insight into the molecular basis of certain types of developmental disability and ASD, and have identified a novel class of targets for the development of therapeutics for the treatment of individuals with ASD.

153.004 Targeted Treatments in Fragile X Syndrome. S. Jacquemont*¹, A. Curie², V. des Portes³, M. G. Torrioli⁴, E. Berry-Kravis⁵, R. Hagerman⁶, F. J. Ramos⁷, K. Cornish⁸, Y.

He⁹, C. Paulding⁹, G. Neri¹⁰, F. Gasparini¹¹, A. Floesser¹², J. Branson¹¹, G. Bilbe¹¹, D. Johns¹³ and B. Gomez-Mancilla¹³, (1)University Hospital of Lausanne, University of Lausanne, (2)Hospices Civils de Lyon, Université de Lyon and CNRS, (3)Hospices Civils de Lyon, Université de Lyon and CNRS UMR 5230 (L2C2), (4)Università Cattolica del Sacro Cuore, Cattedra di Neuropsichiatria Infantile, (5)Rush University Medical Center, (6)UC Davis MIND Institute, (7)Department of Pediatrics, University of Zaragoza Medical School, (8)School of Psychology, Psychiatry, & Psychological Medicine, (9)Biomarker Development, Novartis Institutes for Biomedical Research, (10)Università Cattolica del Sacro Cuore, Istituto di Genetica Medica, (11)Neuroscience Discovery, Novartis Pharma AG, (12)Neuroscience Clinical Sciences and Innovation, Novartis Institutes for Biomedical Research, Novartis Pharma AG, (13)Neuroscience Translational Medicine, Novartis Institutes for Biomedical Research, Novartis Pharma AG

Fragile X syndrome (FXS) is caused by expansion of a CGG repeat in the 5' untranslated region of the fragile X mental retardation 1 (FMR1) gene. This mutation is associated with hypermethylation at the FMR1 promoter and subsequent transcriptional silencing. The absence of FMRP (FMR1 protein) at the synapse has many consequences, including up-regulation of metabotropic glutamate receptor 5 (mGluR5)-mediated signaling. It has been postulated that this increased mGluR5 signal may be responsible for many of the clinical manifestations observed in fragile X syndrome. mGluR5 receptor antagonists have repeatedly been shown to rescue many phenotypes and endophenotypes in animal models of the fragile X syndrome. Comprehensive phenotype correction also occurs when treatment is administered later in the adult KO mice. We examined whether a receptor subtype-selective inhibitor of mGluR5, AFQ056, improves the behavioral symptoms of FXS in a randomized, double-blind, two-treatment, two-period, crossover study of 30 male FXS patients aged 18 to 35 years. We detected no significant effects of treatment on the primary outcome measure, the Aberrant Behavior Checklist-Community Edition (ABC-C) score, at day 19 or 20 of treatment. In an exploratory analysis, however the patients with full FMR1 promoter methylation and no detectable FMR1 messenger RNA improved, as measured with the ABC-C, significantly more after AFQ056 treatment than with placebo ($P < 0.001$). If confirmed in larger and longer-term studies, these results suggest that blockade of the mGluR5 receptor in patients with full methylation at the FMR1 promoter may show improvement in the behavioral attributes of FXS.

Core Deficits Program

154 Social and Adaptive Functioning

This session examines core deficits in social skills and adaptive behavior focusing on the specificity of these symptoms to ASD, changes across the lifespan, and relation to intellectual functioning.

154.001 Understanding the Relationship Between Friendship Quality and Peer Conflict Following the UCLA PEERS® School-Based Curriculum. M. M. Wasserman^{*1}, M. K. Kalies², R. Ellingsen³, Y. Bolourian⁴ and E. Laugeson⁵, (1)Pepperdine University, (2)UCLA PEERS Clinic, (3)University of California Los Angeles, (4)The Help Group - UCLA Autism Research Alliance, (5)UCLA Semel Institute for Neuroscience & Human Behavior

Background:

Deficits in social skills are a hallmark feature among individuals with Autism Spectrum Disorders (ASD), with the friendships of youth with ASD differing from those of their neurotypical counterparts (Bauminger, Solomon and Rogers, 2010). Adolescents with ASD often have more impaired friendship quality than their neurotypical peers, and their friendships may also be more prone to conflict (Bauminger and Kasari, 2000). The Program for Education and Enrichment of Relational Skills (PEERS®), a parent-mediated, evidence-based group social skills intervention assists in developing and maintaining friendships for middle school and high school youth with ASD. Previous research investigating the efficacy of PEERS® reveal significant improvements in friendship quality post-treatment (Laugeson et al., 2009; Laugeson et al., 2012); however, the relationship between friendship quality and degree of conflict during social interactions post-treatment has yet to be examined.

Objectives: This study aims to understand the relationship between adolescent self-reported friendship quality and the degree of conflict during social engagements with peers following the implementation of a 14-week intervention (PEERS®).

Methods:

Under the auspices of The Help Group – UCLA Autism Research Alliance, 146 middle and high school students with ASD ranging from 11-18 years of age ($M=15.08$; $SD=1.802$) participated in a larger treatment outcome study investigating the effectiveness of a teacher-facilitated, parent-assisted PEERS® curriculum in a non-public school

setting. Adolescent participants received daily social skills instruction in the classroom for 20-30 minutes, five days per week, for 14 weeks. Instruction was provided by the classroom teachers who were trained and supervised on the intervention. Parents were invited to participate in weekly 90-minute meetings that taught them strategies to assist their teens in improving their friendship skills. Treatment outcome measures included the adolescent-reported Friendship Qualities Scale (FQS; Bukowski, Hoza, & Boivin, 1994) and the Quality of Socialization Questionnaire for Adolescents (QSQ-A; Frankel & Mintz, 2008), as well as the parent-reported Quality of Socialization Questionnaire for Parents (QSQ-P; Frankel & Mintz, 2008). Both the QSQ-A and QSQ-P assess the degree of conflict during get-togethers with peers. In order to understand the relationship between friendship quality and peer conflict during social interactions, the present study examined post-treatment adolescent self-reported friendship quality on the FQS and post-treatment self- and parent-reported conflict during get-togethers as measured by the QSQ-A and QSQ-P.

Results:

Results reveal that higher post-treatment scores on the FQS in the areas of adolescent self-reported companionship ($p < .001$), closeness ($p < .05$), and overall friendship quality ($p < .05$) predict less teen-reported conflict during get-togethers on the QSQ-A. In addition, higher scores on the FQS in the areas of teen-reported companionship ($p < .01$), security ($p < .05$), and overall friendship quality ($p < .05$) predict less parent-reported conflict during adolescents' get-togethers on the QSQ-P.

Conclusions:

Results suggest that greater friendship quality as perceived by adolescents is related to less conflict during social interactions as perceived by parents and adolescents following a 14-week parent-assisted social skills intervention. These findings also indicate that increased companionship, closeness, and security in friendships are inversely related to conflict in peer relationships for adolescents with ASD.

154.002 Relationship Between Self-Concept and Peer Victimization Amongst Adolescents with Autism Spectrum Disorders. A. R. Dillon*¹, R. Ellingsen², J. Hopkins³ and E. Laugeson⁴, (1)*Pacific Graduate School of Psychology*, (2)*University of California Los Angeles*, (3)*UCLA PEERS Clinic*, (4)*UCLA Semel Institute for Neuroscience & Human Behavior*

Background: According to the National Center for Educational Statistics, 28% of adolescents reported being the victims of bullying within a six-month period (Robers, Zhang, & Truman, 2010). This number nearly doubles for adolescents with special needs. Adolescents with Autism Spectrum Disorders (ASD) are known to be frequent targets of bullying and victimization (Little, 2002). Klin et al. (2000) describe individuals with ASD as "perfect victims" for bullying due to their social deficits. Moore and Kirkham (2001) found that individuals who reported being victims of bullying had significantly lower self-esteem when compared to individuals who reported never being bullied. Additionally, the more the individual reported victimization, the lower their self-esteem. While much of the current research in this area examines the relationship between self-concept and victimization among typically developing youth, little is known about the impact of peer rejection and victimization for adolescents with ASD.

Objectives: This study seeks to investigate the relationship between adolescent self-report of peer victimization and self-concept among teens with ASD. Correlations between adolescent's self-concept and self-perceived peer victimization on three standardized measures were examined.

Methods: Participants included 47 adolescents with ASD ranging from 11-17 years of age ($M = 13.62$; $SD = 1.71$) referred for social skills treatment. Participants completed the Social Skills Improvement System (SSIS; Gresham & Elliot, 2008), Olweus Bullying Questionnaire (OBQ; Olweus, 1996) and Piers-Harris Self-Concept Scale-2 (PHS-2; Piers & Herzberg, 2002) prior to treatment. Adolescent responses from the PHS-2, SSIS Bullying Subscale, and one question from the OBQ that explicitly inquired how often the adolescent had been bullied were examined using Pearson correlations in order to understand the relationship between adolescent self-perceived peer victimization and self-concept.

Results: Results reveal a significant correlation between the PHS-2 Total score, which measures overall self-esteem, and the SSIS Bullying Subscale ($r = -.445, p = .002$). To determine which subscales on the PHS-2 correlated with self-perceived victimization, additional correlations were conducted. Significant correlations between endorsement of victimization on the SSIS Bullying Subscale and the PHS-2 subscales were revealed in the areas of Behavioral Adjustment ($r = -.631, p = .000$), Freedom from Anxiety ($r = -.487, p = .001$), and Happiness and Satisfaction ($r = -.356, p = 0.14$). The correlation between the PHS-2 Total score and the OBQ item relating to frequency of bullying was not significant ($r = -.194, p = .202$).

Conclusions: Results reveal that adolescents who endorse greater overall peer victimization also report more problematic behaviors, more anxiety, and are less happy and less satisfied with their lives. This study highlights the need for increased mental health services to address peer victimization and bullying for adolescents with Autism Spectrum Disorders in order to decrease problematic behaviors, reduce anxiety, and improve overall happiness and life satisfaction.

154.003 Virtual Social-Attention, Anxiety and ADHD in Older Children with ASD. P. C. Mundy^{*1}, W. Jarrold¹, J. Bailenson², M. Gwaltney³, N. McIntyre⁴, N. V. Hatt⁵, M. Solomon⁶ and K. Kim⁷, (1)UC Davis, (2)Stanford University, (3)University of California Davis, Learning & Mind Sciences, (4)U.C. Davis, (5)University of California at Davis, (6)Department of Psychiatry, MIND Institute, Imaging Research Center, (7)MIND Institute, UC Davis

Background: Atypical social attention is a cardinal feature of Autism Spectrum Disorders (ASD). However, our understanding of social attention in school aged children with ASD is less precise than in preschool children. The former would benefit from the application of measures of types of social-attention that matures between 8 to 18 year-of-age and from research that examines the possible moderators of attention in ASD, such as social anxiety or ADHD.

Objectives:

This paper describes a new paradigm for social attention research that assesses social orienting and attention disengagement to social partners in a virtual-reality public speaking task. Two studies

of 91 children will be presented that examine the sensitivity of this paradigm to diagnostic group differences in 8- to 16-year-olds. The studies also examine the hypothesis that social versus object-oriented attention is more sensitive to diagnostic group differences, and that social anxiety and ADHD symptoms moderate performance group differences in social attention.

Methods:

37 higher functioning children with ASD (11.92 years, $SD = 1.2$) and 54 children with typical development (11.75 years, $SD = 1.1$) were participants. The group Full Scale IQs were 108 (16.3) and 116 (14.84) for the ASD and TD samples respectively. Parent report on the Conners-3 ADHD and child self-report on the Multidimensional Anxiety Scale for Children (MASC) were obtained. Children were presented with two 3-minute trials in a 360 degree, 3D virtual classroom populated by 9 peers (avatars) at a classroom table. The children responded to concrete questions about themselves while attempting to direct attention to the faces of each of the avatars on each trial. Five *Frequency of Looks*, and *Average Duration of Look* scores were calculated for the Central Avatar (CA) and pairs of Avatars 1, 2, 3, or 4 positions to the left or Right of CA.

Results:

The Frequency of Looks measures, but not the attention duration measures, displayed diagnostic group sensitivity and specificity of 76% and 74%, ($p < .004$). A Diagnostic Group by Avatar Position quadratic interaction for the Five Frequency of Looks revealed that significant group differences occurred for avatar positions 2 and 3 Left/Right of CA, $F(1,74) = 9.96, p < .002, \eta^2 = .12$. More robust group differences were observed with social versus non-social avatars $F(1, 41) = 8.50, p < .006, \eta^2 = .17$. Finally, Social Anxiety and ADHD interacted and moderated social attention in the HFA sample, $(1, 23) = 5.81, p < .025, \eta^2 = .20$.

Conclusions:

The results indicate that virtual public speaking tasks may offer a new paradigm for delving more

deeply into the course of ASD related developmental impairment in social attention in school aged children. The results are consistent with previous findings on the maintenance of more robust social versus non-social attention disturbance in school aged children with ASD. The results also highlight the need to consider complex nature of the moderator processes in fully informative research on the heterogeneous nature of development in ASD.

154.004 Examining the Developmental Trajectory of Social Functioning for Adolescents and Young Adults with ASD. M. N. Park*¹, R. Ellingsen², C. E. Lin¹, A. Gantman¹ and E. Laugeson¹, (1)*UCLA Semel Institute for Neuroscience & Human Behavior*, (2)*University of California Los Angeles*

Background: Although autism spectrum disorders (ASD) are considered lifelong conditions, relatively few studies have examined the developmental course of social functioning beyond early childhood (Orsmond, Krauss, & Seltzer, 2004). In particular, little is known about the differences in social trajectory across adolescence and young adulthood. Because these are critical periods of transition and present unique social demands and expectations for adolescents and young adults with ASD, understanding the differences in social functioning at these developmental stages is essential.

Objectives: The purpose of this study is to investigate the developmental trajectory of social functioning among youth with ASD without intellectual disabilities across early adolescence, later adolescence, and young adulthood.

Methods: Data were collected from 244 adolescents and young adults with ASD seeking social skills treatment to examine differences in social functioning across three developmental time points (middle school, $n = 120$; high school, $n = 60$; post-secondary, $n = 64$). Adolescent and young adult social functioning was assessed prior to treatment via parent/caregiver reports on standardized measures including the Social Responsiveness Scale (SRS; Constantino & Gruber, 2005), Social Skills Rating System (SSRS; Gresham & Elliot, 1990), and Social Skills Improvement System (SSIS; Gresham & Elliot, 2008), as well as youth self-reports on the Social Anxiety Scale (SAS; La Greca, 1998), Quality of Socialization Questionnaire (QSQ; adapted from Frankel et al., 2010), and the Children's

Depression Inventory (CDI; Kovacs, 1992) for adolescents or the Major Depression Inventory (MDI; Bech et al., 2001) for young adults.

Results: Preliminary results reveal several differences in social functioning across these developmental periods. Parent/caregiver reports on the SRS reveal greater impairment in social cognition for young adults at the post-secondary level compared to adolescents in middle school ($p < .05$) and greater impairment at a trend-level for overall social responsiveness and social motivation ($p < .10$) for young adults at the post-secondary level compared to adolescents in middle school. Youth self-reports of social isolation on the QSQ suggest that adolescents in high school experience greater social isolation in comparison to those in middle school ($p < .05$). Finally, young adults at the post-secondary level self-report more depression than adolescents in middle school and high school ($ps < .001$), as well as more social anxiety ($p < .001$) within the context of greater fear of negative evaluation ($p < .01$), social avoidance and distress specific to new situations ($p < .01$), and generalized social avoidance and distress ($p < .001$) than adolescents in middle school.

Conclusions: Results indicate that impairments in social responsiveness and symptoms of depression and anxiety may magnify with age for adolescents and young adults with ASD. Moreover, social isolation may be exacerbated during later adolescence. These preliminary findings support the notion that overall social impairment and psychosocial functioning are likely to worsen with age for transitional youth with ASD.

154.005 Longitudinal Trajectory of Adaptive Behavior in Individuals with Fragile X Syndrome. C. Klaiman*¹, B. Jo², A. A. Lightbody², L. C. Chromik² and A. L. Reiss², (1)*Emory University School of Medicine and Marcus Autism Center*, (2)*Stanford University*

Background: Fragile X syndrome (FraX) is the leading inherited cause of developmental disability. Adaptive behavior, the term used to indicate an individual's ability to independently function in their environment changes over the course of an individual's life. Individuals with FraX have strengths in daily living skills with weaknesses in socialization and communication skills, similar to individuals with autism (ASD). Some reports suggest that there may be changes

in adaptive behavior over time, with different studies showing gains and others declines.

Objectives: The purpose of this study was to examine, prospectively and longitudinally, the adaptive behavior of children with FraX. Specifically, we examined the mean level and rates of development for the Adaptive Behavior Composite score and the domain scores as measured by the Vineland Adaptive Behavior Scales (Vineland). In this large scale study, we investigated the rate of adaptive skill acquisition as well as the adaptive behavior profiles in individuals ages 6 through 16 years.

Methods: The participants were 265 individuals with FraX (186 males, 79 females) and 225 typically developing individuals (124 males, 101 females). All individuals with FraX were diagnosed with full mutation FraX using DNA analyses. The Vineland was used to assess adaptive behavior. Depending on the Vineland domain, 252-265 had one assessment, 186-187 had 2 assessments, 46 had 3 assessments and 6 had 4 assessments. The mean interval between assessments was 1.94 years.

Results: Common growth model was used to estimate trajectories of Vineland domains. The Adaptive Behavior Composite (ABC) score did not change for control males or females or FraX females. FraX males change rapidly from 6-11 years ($p < .001$) but not from 11 – 16 years ($p > .05$). This is similar to results on the socialization domain, though the FraX males continue to show declines through 16 years ($p = .003$). In the communication domain, both control and FraX males decline from 6-11 ($p = .006$ and $p < .001$ respectively). From 11-16 years, all but FraX females decline significantly. With regard to daily living skills, no changes are seen with regard to control individuals however FraX females increased significantly ($p = .04$) and FraX males decreased significantly ($p < .001$) from 6-11 years. Comparing typical trajectories to FraX trajectories, for males the gap in adaptive behavior widens with age.

Conclusions: In this original, large scale, longitudinal study, we were able to elucidate trajectories of adaptive behavior across a wide age range in boys and girls with FraX. Boys with FraX show the largest declines in adaptive

behavior with socialization skills declining the least, albeit continually through 16 years. Communication skills decline the most overall. Interestingly, this profile is different from individuals with idiopathic autism who show the largest declines in socialization and communication skills over time. It is important to be aware of developmental periods where skills are particularly likely to diminish in FraX so that those working with affected individuals can attempt to preserve behavioral sets that are most vulnerable. Understanding developmental trajectories in FraX will also be of value in understanding and interpreting the effects of new treatments for this disorder.

154.006 The Functional Profile of Children with Autism Spectrum Disorders: A Study with the Vineland Adaptive Behavior Scale (VABS) At Different Intellectual Levels Versus Non Autism Population. S. Mougá*¹, J. Almeida², C. Café², F. Duque² and G. Oliveira², (1)*Faculdade de Medicina – Universidade de Coimbra*, (2)*Hospital Pediátrico Carmona da Mota (HP) – Centro Hospitalar e Universitário de Coimbra (CHUC)*

Background: Autism spectrum disorders (ASD) are severe, life-long neurodevelopmental disorders that compromise functioning across multiple domains, including cognitive functioning and adaptive behavior. The relevance of Intellectual Quotient (IQ) to the symptomatic expression of autism and consequent involvement in the subject's personal and social autonomy remains unclear. Therefore, the assessment of adaptive skills is an important factor to diagnostic evaluations, treatment planning and progress monitoring.

Objectives: Our aim is to study the influence of the primary diagnosis of ASD versus other neurodevelopmental disorders (OND) on daily living skills (DLS) besides IQ.

Methods: The sample consisted of 147 school-aged children with ASD (N=73) or OND (N=74). All ASD patients had ADI-R and ADOS positive results. The subjects in the OND group did not meet the clinical criteria for ASD. These two clinical groups were further subdivided, taking into account the classification of intellectual disability (ID) of the CID-9 (ID is present when the IQ < 70), and matched by Full-Scale IQ score. In these four clinical subgroups (ASD with no ID-ASD_NID; ASD with ID-ASD_ID; OND with no ID-OND_NID;

OND with ID-OND_ID) we compared the functional profile by ID (ASD_NID[N=49] vs OND_NID[N=48]; ASD_ID[N=24] vs OND_ID[N=26]), namely in the communication, DLS, socialization and the adaptive behavior composite-ABC-(assessed with the VABS; mean±SD:100±15) to clarify the impact of primary diagnosis in the everyday adaptive skills besides IQ. Statistic analysis (SPSS17) was performed comparing the standard scores of VABS within the two clinical groups and between the four subgroups with Mann-Whitney U test. Significance level(σ)=0.05.

Results: ASD(N=73) and OND(N=74) groups showed similar results in the communication domain of the VABS ($p=.860$), but statistically significant differences in the other domains: DLS, socialization and the ABC ($p<.05$). When we analyzed the four clinical subgroups paired by ID we found a differential profile of standard scores of VABS in DLS (ASD_NID/OND_NID: $p=.028$; ASD_ID/OND_ID: $p<.001$) and socialization (ASD_NID/OND_NID: $p=.001$; ASD_ID/OND_ID: $p=.031$) domains. In these two domains, the OND group had higher standard scores (DLS-mean±SD:ASD_NID-75±11; OND_NID-81±11; ASD_ID-58±11; OND_ID-73±15 and socialization-mean±SD:ASD_NID-78±12; OND_NID-86±10; ASD_ID-66±8; OND_ID-73±12). In the communication domain the only statistical difference was found in the subgroup ASD_ID/OND_ID:($p=.037$). The same happened in the ABC (ASD_NID/OND_NID: $p=.084$; ASD_ID/OND_ID: $p=.002$).

Conclusions: These findings demonstrate that the ASD groups differ negatively from OND groups in the competence of DLS and socialization, despite de same IQ and education opportunity. Given the fact that the social interaction difficulties are one of the core symptoms of ASD, this was an expected result. The true novelty of this study is the fact that the level of autonomy is considerably lower in ASD groups, even when we focus on the group NID. Taken together, these results show that IQ in neurodevelopmental disorders is not the determinant factor for developing adaptive DLS. It is possible to presume that the specific cognitive social deficits in autism in the application of knowledge are a factor that limits adaptive competence for DLS. These results

have significant clinical implications, enhancing the importance of early intervention targeting personal and social autonomy. These preliminary findings should be replicated in a larger sample.

154.007 Relationship Between Adaptive Functioning and Autism Symptom Severity. C. Montiel-Nava^{*1}, Z. Gonzalez², J. A. Chacin¹, J. Pena¹ and E. Solís¹, (1)*La Universidad del Zulia*, (2)*Hospital de Especialidades Pediátricas*

Background: Communication and socialization are adaptive skills which are central for the study of individuals with autism, since impairment in these two domains are the defining features of the disorder. When compared with typically developing children, those with autism have shown greater impairment in their adaptive behavior, even when matched for age and IQ

Objectives: The aim of the present study was to investigate the relationship between adaptive behavior and autistic symptomatology in preschool children with autism. It was predicted that there would be a correlation between autistic symptomatology and adaptive functioning, and that this relationship would be stronger in terms of socialization and communication.

Methods: Age, adaptive skills levels, and autistic symptomatology levels were collected on consecutive participants, as a part of an epidemiological study of autism spectrum disorders at the University of Zulia's Developmental Disorders Clinic. Participants in this study included 52 children with autism aged 3 to 6 years. Children were diagnosed using SCQ scores above 15, algorithm scores from the Autism Diagnostic Observation Schedule (ADOS); and having the diagnosis confirmed by an expert clinician; and parents were interviewed using the Spanish Vineland Adaptive Behavior Scales (VABS). All children in the study met SCQ, ADOS and clinician criteria for autism. Exclusion criteria were: known brain lesions, tuberous sclerosis, neurofibromatosis, hemiparesis, ataxia, or any "hard" neurological sign.

Results: The socialization domain only exhibited significant correlations with the play scores (-0.565), and repetitive/stereotyped behavior (-0.485). The communication domain showed the most correlations with the autistic symptomatology; there were significant negative

correlations with the ADOS social reciprocal interaction (-0.413), the sum of communication and social interaction (-0.387), play (-0.425), and repetitive/stereotyped behavior (-0.641). For the daily living skills domain, the significant correlations were with the play (-0.458), and the repetitive/stereotyped behavior (-0.46). The highest and strongest correlations with all the VABS domains were for the ADOS repetitive/stereotyped behavior scores. All the correlations were significant ($p < 0.01$), indicating negative relationships with the daily living skills (-0.46), socialization (-0.485), and communication (-0.641) domains. Sequential regressions were run for each adaptive behavior domain. For VABS socialization domain, ADOS play score was the most predictive variable accounting for 33% of the variance for this domain. For VABS communication, all the ADOS scores were significant predictors, being the play score the most significant predictor (49.9%), followed by the total sum of communication and reciprocal social interaction (39%). The VABS daily living skills were also best predicted for the stereotyped behavior and restricted interests' scores, contributing to 34% of the variance.

Conclusions: Communication adaptive skills were predictive of all autism symptoms, whereas socialization adaptive skills showed no significant relationship with them. Play and stereotyped behaviors might be an important element in the diagnostic process, since it predicted communication and socialization adaptive behaviors. The findings of this study highlight the need to have a better understanding of the relationships between adaptive behaviors and autism symptoms, so the planning of treatment will have an effect on children's everyday functioning.

154.008 The Role of Racial Diversity: Examining Differences in Parent Report of Adaptive Behavior. B. Brooks^{*1}, K. A. Casagrande¹, L. Herlihy² and D. L. Robins¹, (1)Georgia State University, (2)University of Connecticut

Background:

Cultural and racial socialization significantly impact an individual's worldview and expectations for behavior. Several studies suggest that there is cultural variability in child-rearing practices; parents from different racial backgrounds may employ different strategies and place more

significance on the development of certain skills, which might influence parent-report of child behavior.

Objectives:

This exploratory study investigated differences in parent-report of adaptive behavior in toddlers at risk for autism. Racial differences will be explored while controlling for socioeconomic status, as measured by level of maternal education.

Methods:

Parents completed the M-CHAT(-R) at a pediatric 18- or 24-month well-child visit. Children at risk based on the M-CHAT(-R)+Follow-up (M-CHAT(-R)/F) or whose parents and/or pediatrician expressed concerns about their development were invited to complete a diagnostic evaluation ($N=137$; $M_{age}=26.61$ months, $SD=4.89$). Evaluations consisted of measures of ASD symptomatology, general cognitive skills, and adaptive abilities.

Results:

There was a significant difference in maternal education levels between Caucasian (CA; $N=77$; $M=15.88$, $SD=2.36$) and African-American parents (AA; $N=60$; $M=13.80$, $SD=2.56$), $t=4.95$, $p < .001$. A series of 2x2 between-subjects ANOVAs examined race and diagnosis ($N_{ASD}=75$, $N_{non-ASD}=62$), controlling for maternal education. Results indicated a significant main effect of race on the VABS Communication domain, $F(1, 136)=4.97$, $p=.027$, with African-American parents reporting lower communication skills than Caucasian parents ($M_{AA}=76.92$, $SD=12.10 < M_{CA}=83.23$, $SD=13.25$). There was also a significant main effect of diagnosis on Communication, $F(1, 136)=21.85$, $p < .001$, and Socialization standard scores, $F(1, 136)=11.81$, $p=.001$, with parents of children diagnosed with ASD reporting lower communication ($M_{ASD}=76.25$, $SD=13.50 < M_{non-ASD}=85.56$, $SD=10.63$) and socialization ($M_{ASD}=81.60$, $SD=8.62 < M_{non-ASD}=87.06$, $SD=10.96$) skills. No significant race x diagnosis interactions were observed.

To better understand the significant finding of higher reported communication skills by

Caucasian parents, additional 2x2 ANOVAs examined the influence of expressive and receptive language. There was a main effect of race on receptive language, $F(1,136)=5.20$, $p=.024$ ($M_{CA}=12.45$ $SD=2.99$ > $M_{AA}=10.98$, $SD=2.60$), but not on expressive language, $F(1,136)=1.49$, $p=.224$.

Conclusions:

Although the main effect of diagnosis on communication and socialization is to be expected, the more interesting findings lie in the main effect of race on communication skills. The difference in communication across racial categories was driven by receptive language, and not by expressive language skills. It is possible that this may be due to different cultural expectations in listening skills. It is important to investigate other factors which may contribute to differences in parent perception outside of race and SES, such as number of children or marital status.

Genetic Factors in ASD Program

155 Genetics

155.001 Impact of Pathogenic Structural Variants On Gene Expression in ASD. D. H. Geschwind^{*1}, R. Luo² and Y. Tian³, (1)*David Geffen School of Medicine at UCLA*, (2)*UCLA*, (3)*University of California Los Angeles*

Background:

Genetic factors contribute significantly to Autism Spectrum Disorders, yet no single genetic factor accounts for more than 1% of ASD cases, indicating significant heterogeneity. This leads to the question: Is autism a heterogeneous collection of hundreds of distinct, individually rare conditions, or are there common pathways into which these rare conditions can be grouped?

Objectives:

To provide an overview of gene expression studies in ASD, which provide a genome-wide, relatively unbiased assessment of pathway convergence in ASD.

Methods:

We performed gene expression in blood and brain using microarrays, and in some cases RNAseq and used multiple types of analyses to assess convergence. One method uses an "outlier analysis" approach to identify gene expression changes associated with certain individual pathogenic mutations in the Simons Simplex Collection (e.g. Luo et al. 2012 AJHG) and in AGRE. This method is based on the assumption that ASD is a collection of rare disorders. Another approach involves direct comparison between blood or lymphoblast gene expression in probands versus siblings as a group. This method is implicitly searching for some common shared risk among probands. Finally, we have performed gene expression profiling in brain, using multiple analytic methods to define the molecular pathology and gene expression networks associated with ASD.

Results:

Outlier analysis shows that genes dysregulated in probands, but not in unaffected siblings, are enriched in development/ neurogenesis/ synaptogenesis (neural related pathways; $p = 9.54E-03$), and synaptic cell adhesion ($p = 2.0E-02$). Some of these same pathways are altered in brain gene expression studies and in our study of gene expression in lymphoblasts focusing on monogenic chromosomal disorders that increase risk for ASD. These data suggest a very strong peripheral signal in rare, monogenic forms of ASD, including del(16p) and dup(22q). When we take the approach that searches for common derangements of expression across ASD, we find that the signal separating cases from controls is much less strong than when using the rare variant approach. This is consistent with GWAS studies that show no strong individual SNP effects, but an overall skewing of association, which favors the contribution of multiple small variants of small effect. Finally, overlapping the brain data with the blood data identifies a few genes that are differentially expressed in ASD in both cases.

Conclusions:

Rare pathogenic structural variants cause significant transcriptomic changes that converge on neural pathways, even in peripheral blood. Similarly, gene expression in brain suggests convergent molecular processes might link cases

of ASD with distinct molecular etiologies. This may have significant implications for therapeutic development.

155.002 A Long Noncoding RNA, *MSNP1AS*, Contributes to ASD Risk. T. K. Kerin, A. Ramanathan, K. Rivas, N. Grepo, G. A. Coetzee and D. B. Campbell*, *University of Southern California*

Background: Twin concordance and sibling recurrence rates suggest a strong contribution of genetic factors to autism spectrum disorder (ASD) risk. However, the genetics of ASD have proven to be complex. Genome-wide association studies (GWASs) are designed to identify novel genes and pathways that contribute to complex disorder risk. Application of GWAS techniques to ASD identified genetic markers with genome-wide significant association on chromosomes 5p14.1, 5p15.2, and 20p12.1. Association of the chromosome 5p14.1 marker rs4307059 with ASD diagnosis was replicated in an independent sample. Further, rs4307059 was associated with social communication phenotypes in a general population sample, providing additional evidence that this chromosome 5p14.1 genetic signal contributes to ASD-related phenotypes. Although widely interpreted as implicating the nearest protein-coding genes, cadherin 9 (*CDH9*) and cadherin 10 (*CDH10*), the original GWAS publication reported a lack of correlation between rs4307059 genotype and brain expression of the cadherins.

Objectives: To determine the biological basis of the chromosome 5p14.1 GWAS peak.

Methods: Bioinformatics approaches identified a single noncoding RNA directly under the chromosome 5p14.1 GWAS peak. Northern hybridization confirmed expression of the ~4 kb noncoding RNA, *MSNP1AS* (moesin pseudogene 1, antisense), and indicated that *MSNP1AS* binds the transcript of the X chromosome protein-coding gene moesin (*MSN*). Quantitative PCR (qPCR) was used to determine expression levels of *MSNP1AS*, *MSN*, *CDH9* and *CDH10* in 10 pairs of autism-control postmortem temporal cortex samples. Transfection of a *MSNP1AS* over-expression construct into human neuronal cells was followed by Western blot analysis of moesin protein.

Results: Expression of the noncoding RNA *MSNP1AS* was increased 12.7-fold ($P=0.004$) in postmortem temporal cortex of individuals with ASD compared to controls. Further, increased expression of *MSNP1AS* in postmortem temporal cortex was correlated with the ASD-associated rs4307059 genotype. Consistent with previous microarray reports, expression levels of the nearest protein-coding genes, *CDH9* and *CDH10*, were not altered in ASD temporal cortex. Confirming results in the original GWAS report, we also found that expression levels of *CDH9* and *CDH10* were not correlated with rs4307059 genotype, suggesting that the ASD genetic association signal does not implicate the cadherins. Expression of the X chromosome gene *MSN* was increased 2.4-fold ($P=0.029$). Despite the significantly increased *MSN* RNA, moesin protein levels were not increased in postmortem temporal cortex of individuals with ASD, suggesting that the noncoding RNA *MSNP1AS* may play a role in reducing moesin protein. To test this hypothesis, we over-expressed *MSNP1AS* in a human neuronal cell line. Western blot analysis indicated a significant 40% decrease in moesin protein, establishing that *MSNP1AS* negatively regulates moesin protein expression.

Conclusions: We identified a previously uncharacterized noncoding RNA, *MPSNP1AS*, which represents an ASD candidate gene with genome-wide significant association, functional correlation with the ASD-associated genetic allele, and a large increase in expression in postmortem ASD temporal cortex. *MSNP1AS* binds *MSN*, and over-expression of *MSNP1AS* causes a decrease in moesin protein. This ongoing work represents the critical post-GWAS translation of genetic findings to an understanding of their biological consequences and highlights the potential contributions of noncoding RNAs to ASD risk.

155.003 Whole-Exome and CNV Data for ASD Sex Bias. S. J. Sanders* and M. W. State, *Yale University School of Medicine*

Background: The predominance of male cases is amongst the most striking, consistent and unexplained observations in ASD. Recent papers have repeatedly highlighted the importance of *de novo* variants in ASD causation and these variants have been used to identify specific risk loci (e.g. 16p11.2, *SCN2A*). In this presentation we will consider what *de novo* and rare variation can

contribute to understanding of the genomic architecture and mechanisms of ASD sex bias.

Objectives: To characterize how the distribution of *de novo* and rare variants in ASD probands differs between the sexes and to assess whether this data supports specific models of ASD sex bias.

Methods: Samples from the Simons Simplex Collection were analyzed by genotyping array (N=2,326 families; 309 female probands, 2,017 male probands) and whole-exome sequencing (N=964 families; 147 female probands; 761 male probands) to identify *de novo* and rare variants predicted to alter protein composition.

Results: Female probands consistently show a higher proportion of *de novo* variants than their male counterparts for both CNVs and loss of function (LoF, i.e. nonsense, canonical splice site and frameshift variants) variants. For *de novo* CNVs that include exons the difference is modest (9.1% of females vs. 5.4% of males, OR 1.76 (95% CI: 1.11-2.78), $p=0.01$), however considering only *de novo* CNVs implicated in clinical syndromes, such as 16p11.2, leads to a difference of a similar order to the sex bias observed in ASD (4.9% of females vs. 1.4% of males, OR 3.26 (95% CI: 1.82-7.14), $p<0.001$). From whole-exome sequencing a similar pattern emerges with a higher rate of *de novo* LoF in females (22.4% of females vs. 10.6% of males; OR 2.4 (95% CI 1.5-3.9), $p<0.001$); a similar non-significant trend is observed when the analysis is restricted to genes with ≥ 2 *de novo* LoF (a threshold at which they are considered ASD-associated) though only 21 individuals have such variants (4.1% of females vs. 2.0% of males; OR 2.12 (95% CI: 0.72-5.94), $p=0.13$). Finally while *de novo* CNV and LoF variants are observed on chrX, they are not seen at a greater rate than on other chromosomes.

Conclusions: In individuals diagnosed with ASD, risk-associated *de novo* variants occur more often in females than in males. Such an observation is consistent with a model of relative protection to ASD liability in females, but with the caveat that *de novo* events contribute sufficient risk that the protective mechanism is overwhelmed. In such a model the increase in *de novo* events is the consequence of a smaller proportion of females in

whom ASD is caused by low risk inherited variation to which the females have protection. This model would explain the comparative similarity in recurrence rate of siblings to male and female probands (the 'Carter Effect'). In summary the observation of increased *de novo* events in females with ASD supports a model of protection to inherited genetic risk in females.

155.004 Identification of Common Epigenetic Alterations in Autism.
A. P. Feinberg^{*1}, C. Ladd-Acosta¹, N. Parikshak², A. R. Runarsson¹, K. D. Hansen¹, R. Irizarry¹, M. D. Fallin³, W. E. Kaufmann⁴ and D. H. Geschwind⁵, (1)Johns Hopkins University, (2)UCLA, (3)Johns Hopkins School of Public Health, (4)Boston Children's Hospital, (5)David Geffen School of Medicine at UCLA

Background: Although autism has a strong heritable component, there is growing evidence for an environmental contribution. Epigenetics is a mechanism for integration of environmental and genetic signals in the development of disease. We have pioneered the field of epigenetic epidemiology, bringing biological, genomic, epidemiological, statistical, and clinical approaches together in a comprehensive and integrated way.

Objectives: To identify epigenetic alterations in autism spectrum disorders (ASD), we examined 41 post-mortem brain samples from cases and controls, focused on 3 brain regions, as well as blood samples from 8 ASD-discordant monozygotic twins.

Methods: We developed new tools for genome-scale epigenetic analysis, including array-based and whole genome bisulfite sequencing, and applied these to the study of ASD. These include robust statistical approaches to the Illumina 450K DNA methylation array such as "bump hunting," and novel approaches to whole genome bisulfite sequencing (WGBS). These will likely be of significant value to others in the field.

Results: 65 autism-related differentially methylated regions (DMRs) were identified, with statistical significance (genome-wide FWER < 0.01 or replication nominal $P < 0.05$) and magnitude of methylation change greater than 5%. Replicating, statistically significant differences involved genes and/or pathways related to genes with mutational mechanisms reported at much lower frequency.

Conclusions: The DMRs identified in the first phase of this research represent the first set of genomic regions commonly altered in ASD, and the biological targets identified are plausible autism candidates. The frequency of alteration is much higher than that of mutational variation, suggesting that epigenetic changes may explain a much higher fraction of ASD than conventional mutation acting alone. The results of this study open the door to novel diagnostic and therapeutic approaches to common autism.

155.005 Characteristics and Predictive Value of Blood Transcriptome Signature in Males with Autism Spectrum Disorders. S. W. Kong*, *Children's Hospital Boston / Harvard Medical School*

Background: Autism Spectrum Disorders (ASD) is a spectrum of highly heritable neurodevelopmental disorders in which known mutations contribute to disease risk in 20% of cases.

Objectives: Here, we present the results of the largest blood transcriptome study to date that aims to identify differences in 170 ASD cases and 115 age/sex-matched controls and to evaluate the utility of gene expression profiling as a tool to aid in the diagnosis of ASD.

Methods: We performed the largest blood gene expression study to date of ASD, designed specifically to provide insight into the performance of a blood expression signature that classifies children with ASD from controls, particularly after an increased index of suspicion based on parent and/or pediatric assessment. Validation of this signature utilized an additional cohort for assessment of classification accuracy.

Results: The differentially expressed genes were enriched for the neurotrophin signaling, long-term potentiation/depression, and notch signaling pathways. We developed a 55-gene prediction model, using a cross-validation strategy, on a sample cohort of 66 male ASD cases and 33 age-matched male controls (P1). Subsequently, 104 ASD cases and 82 controls were recruited and used as a validation set (P2). This 55-gene expression signature achieved 68% classification accuracy with the validation cohort (area under the receiver operating characteristic curve (AUC): 0.70 [95% confidence interval [CI]: 0.62-0.77]). Not surprisingly, our prediction model that was

built and trained with male samples performed well for males (AUC 0.73, 95% CI 0.65-0.82), but not for female samples (AUC 0.51, 95% CI 0.36-0.67). The 55-gene signature also performed robustly when the prediction model was trained with P2 male samples to classify P1 samples (AUC 0.69, 95% CI 0.58-0.80).

Conclusions: Our result suggests that the use of blood expression profiling for ASD detection may be feasible. Further study is required to determine the age at which such a test should be deployed, and what genetic characteristics of ASD can be identified.

155.006 Whole Genome Sequencing in Autism Identifies Hotspots for De Novo Germline Mutation. J. J. Michaelson¹, Y. Shi², M. Gujral¹, H. Zheng³, D. Malhotra¹, T. E. Gadamski⁴, J. A. Estabillio⁵, C. Corsello⁶, N. Akshoomoff⁶, Y. Li³, L. M. Iakoucheva¹, J. Wang³ and J. Sebat*¹, (1)*University of California San Diego*, (2)*BGI Shenzhen*, (3)*BGI-Shenzhen*, (4)*Autism Discovery Institute*, (5)*UCSD & Rady Children's Hospital*, (6)*University of California, San Diego*

Background:

De novo mutation (DNM) plays an important role in Autism Spectrum Disorders (ASDs). Notably, pathogenic copy number variants (CNVs) are characterized by high mutation rates. We hypothesize that hypermutability is a property of ASD-associated genes, and may also include nucleotide-substitution hotspots.

Objectives:

We investigated global patterns of germline mutation by whole genome sequencing of monozygotic twins concordant for ASD and their parents. The goal of this study was to characterize regional mutation rates, identify hotspots for *de novo* mutation and characterize patterns of mutability with respect to functional elements in the genome.

Methods:

Whole genome sequencing (40X coverage, 500 bp library, 90 bp reads) was performed on ten identical twin pairs concordant for ASD and their parents. Raw sequence files were processed at UCSD with a WGS pipeline consisting of automated tools for alignment and variant calling

(BWA, Samtools, GATK 1.2-52). DNM detection was performed using a machine-learning based method forestDNM developed in our laboratory.

Results:

Germline de novo mutations (DNMs) displayed a non-random positioning in the genome ($P < 10^{-4}$). Dense clusters of DNMs (<100 kb apart) could be explained by compound mutation or gene conversion. Clustering on larger scales could be explained by mutation-rate variation throughout the genome. Rates of nucleotide substitution varied by >100-fold, and could be explained by intrinsic characteristics of DNA sequence and chromatin structure. Hypermutability was a characteristic of highly-conserved sequences, particularly of essential genes and genes involved in human disease. In addition, genes impacted by DNMs in this study were significantly associated with autism in independent exome-sequencing datasets.

Conclusions:

Our findings suggest that regional hypermutability is a significant factor shaping patterns of genetic variation and disease risk in humans.

155.007 Simons VIP: Expanding the Characterization of the 16p11.2 Duplication Syndrome. A. V. Snow¹, L. Green-Snyder¹, R. Bernier², R. P. Goin-Kochel³, F. K. Miller¹, J. E. Olson¹, K. Porche¹ and E. Hanson*⁴, (1)*Boston Children's Hospital*, (2)*University of Washington*, (3)*Baylor College of Medicine*, (4)*Children's Hospital Boston*

Background:

Twin and family studies suggest that genetic and/or epigenetic factors are important in the development of ASD, although it is also clear that these influences are complex. Much past work in this field has been marred by inconsistent diagnostic methodology and poorly defined subject populations, which make it challenging to link particular genes to clinical subtypes.

While the exact incidence of ASD in individuals with 16p11.2 duplication is unknown, ASD and ASD-like features appear to be more prevalent in these individuals than in the general population. Increased incidence of ADHD has been reported in individuals with 16p11.2 duplication (Shinawi et

al. 2009). There are also reports of increased incidence of psychiatric disorders, particularly schizophrenia (McCarthy et al. 2009, Levinson et al. 2011). In addition, there have been reports of specific neurological findings in these individuals (Horev et al. 2011, Bedoyan et al. 2010). The Simons VIP is continuing to define the 16p11.2 duplication phenotype by investigating over 100 individuals with this recurrent genetic disorder

Objectives: To expand the characterization of the 16p11.2 duplication syndrome.

Methods: Subjects are recruited from across the United States through the Simons VIP Connect website, and travel to the clinical sites for a 2-3 day research visit. All consenting participants with a documented duplication in 16p11.2 receive a comprehensive diagnostic assessment including an Autism Diagnostic Observation Schedule (ADOS), a DISC (Diagnostic Interview Schedule for Children), cognitive, language, behavioral and adaptive skills assessments. The Autism Diagnostic Interview – Revised (ADI-R) is administered when appropriate. Comprehensive medical history information is obtained from participant report, and is also extracted from medical records.

Results: To date, we have enrolled 37 individuals (from 29 families) with a 16p11.2 duplication, all of whom are included in this interim analysis.

Within the duplication sample, 19 participants were male (51.4%). Probands ranged in age from 7 months to 15 years, and had a mean IQ of 74.0 (SD = 22.3). Four (11%) individuals received a diagnosis of an ASD.

The most common diagnoses were Developmental Coordination Disorder (n = 15), Language Disorders (n = 11), Phonological Disorder (n = 7) and Borderline Intellectual Functioning (n = 7). Other common diagnoses included Intellectual Disability (n = 7), and ADHD (n = 8). Only five individuals received no co-morbid diagnoses. Additional analyses will be conducted to look at specific symptom profiles and compare those profiles to individuals in the Simons Simplex Collection.

Conclusions: Among individuals with a 16p11.2 duplication, co-morbid diagnoses were extremely common, with 32 (86.5%) participants receiving one or more diagnoses in addition to 16p11.2 duplication. Several individuals had motor and/or language delays.

Brain Imaging Program 156 Brain Imaging

156.001 Increased Ratio of Short to Long Range Structural Connections in the BRAIN in ASD – the Relationship Between Grey- and White-Matter Wiring. C. Ecker^{*1}, E. Daly², C. M. Murphy³, M. Gudbrandsen¹, N. Gillan³, M. AIMS³, M. Catani¹ and D. G. Murphy⁴, (1)*Institute of Psychiatry*, (2)*King's College London, Institute of Psychiatry*, (3)*King's College London, Institute of Psychiatry*, (4)*Institute of Psychiatry, King's College London*

Background: Evidence suggests that Autism Spectrum Disorder (ASD) is accompanied by atypical structural brain connectivity. More specifically, it is thought that the brain in ASD is over-connected locally and under-connected globally. However, while evidence for global under-connectivity is growing (e.g. (Koshino et al., 2008; Pugliese et al., 2009)), there is currently a lack of imaging markers that could be used to assess local grey-matter wiring in the brain *in vivo*. Such local grey-matter connections are predominantly located in the outer layers of the cortex (layer 1-3), while the inner layers (layer 4-6) mainly contain myelinated axons extending into white matter (Lewis, Melchitzky, & Burgos, 2002).

Objectives: Here, we therefore examined (1) the ratio between the outer (i.e. pial) and inner (i.e. white-matter) cortical surface as a surrogate marker of the proportion of short-range (i.e. local) to long-range (i.e. global) connections in the brain of individuals with ASD; and (2) established the relationship between atypical grey-matter wiring and white-matter connectivity within the frontal lobes.

Methods: Structural MRI and DTI data was collected on 51 well-characterized male adults with an ADI-R confirmed diagnosis of ASD (mean age = 26 years, mean FSIQ = 112), and 51 age/FSIQ matched neurotypicals. Surface reconstructions for all participants were performed using FreeSurfer software on the basis of high-resolution structural T₁-weighted inversion

recovery images. The ratio between outer (i.e. pial) and inner (i.e. white-matter) surface was computed at each cerebral vertex, and subsequently compared between groups using a general linear model. In addition, we performed DTI tractography of association tracts within the frontal lobe, and determined their mean diffusivity, fractional anisotropy and number of streamlines.

Results: We found that the ratio of outer to inner surface area was significantly increased in individuals with ASD in the bilateral frontal and temporal lobes ($p < 0.05$, corrected). The increase in ratio was further correlated with the severity of autistic symptoms in the social domain. Overall, the ratio of outer to inner frontal surface area was significantly correlated with the mean diffusivity and the number of streamlines of frontal association tracts, which were significantly increased/reduced (respectively) in ASD.

Conclusions: Our results suggest that individuals with ASD may have a larger proportion of short-to long-range connections in frontal and temporal regions, and hence confirm the hypothesis that the brain may be over-connected locally and under-connected globally in ASD. Furthermore, the significant association of grey- and white-matter connectivity implies that global white-matter under-connectivity in ASD should not be examined in isolation (i.e. without consideration of grey-matter wiring), and may be secondary to the abnormal development of grey-matter.

156.002 Oxytocin's Impact On Core Brain and Behavioral Features of ASD in Children. I. Gordon^{*1}, R. H. Bennett², C. Cordeaux¹, M. V. Lucas¹, B. C. Vander Wyk¹, J. F. Leckman¹, R. Feldman³ and K. A. Pelphrey¹, (1)*Yale University*, (2)*Yale Child Study Center*, (3)*Bar-Ilan University*

Background: The effects of the neuropeptide oxytocin (OT) on a wide range of social behaviors in humans, especially increased sociability, empathy, and theory of mind, provide exciting new potential avenues of exploration for Autism Spectrum Disorders (ASD). Discoveries regarding links between variations in the OT receptor gene and ASD prevalence also highlight the need to assess OT's impact on both brain and behavior in ASD. Considering the core social dysfunction in ASD, it is crucial to reach a deeper understanding of OT's behavioral impact, as well as the mechanisms underlying OT's effects using

functional magnetic resonance imaging (fMRI) in children and adolescents with ASD.

Objectives: Employing a developmental perspective, we aimed to identify the impact of OT on brain regions linked to social motivation, social perception, and social cognition. We also aimed to describe the behavioral impact linked with OT administration in scan-related tasks, as well as in naturalistic social interaction settings. We hypothesized that in fMRI tasks that require processing of social information, OT administration will result in increased activity in regions that play a key role in reward circuitry and key nodes of the social brain. We also expected increased connectivity between these brain regions due to OT's impact. Finally, we expected aspects of social behavior, such as eye gaze pattern and positive affect, during interactions with participants' parents to become more synchronized with the social partners' cues after OT administration.

Methods: In the largest study to date (N=20), children with ASD (ages 7-18) were administered an age-appropriate dose of OT. In this double-blind, placebo-controlled study of changes in brain activity after a single dose of OT, we utilized two well-validated fMRI paradigms: Reading the Mind in the Eyes (RMET-R) and Biological Motion Detection. Following administration and prior to the fMRI scan, children and their parents also participated in a videotaped positive interaction paradigm (later to be micro-coded for social behaviors).

Results: Results indicated that administration of OT nasal-spray resulted in increased activity in brain regions known to process social information; specifically, the anterior cingulate and prefrontal cortex, the superior temporal sulcus, temporal parietal gyrus, fusiform, and amygdala. All of these regions have previously been implicated in their involvement in social perception and cognition, mentalizing abilities, and theory of mind. Similar results emerge in several tasks that involve multiple social information processing routes, thus, emphasizing the potential impact of OT beyond a single task. We will also present first-ever reported behavioral outcomes micro-analyzed from videotaped parent-child interactions.

Conclusions: These results provide the essential steps in devising more effective combination treatments for core social deficits in ASD, which may involve grouping validated clinical interventions with OT administration. Such a treatment approach will fundamentally improve our understanding of autism and its treatment.

156.003 Longitudinal Analysis of the Corpus Callosum in Preschool-Aged Children with Autism Spectrum Disorder. C. W. Nordahl*¹, G. S. Young¹, L. M. Perry², R. F. Dougherty², A. Lee³, D. D. Li³, S. Liston¹, T. J. Simon¹, S. J. Rogers³, B. A. Wandell² and D. G. Amaral³, (1)UC Davis MIND Institute, (2)Stanford University, (3)University of California Davis Medical Center

Background: The neuropathology of autism spectrum disorder (ASD) likely involves abnormalities in white matter structure and connectivity patterns. The corpus callosum is of interest because it comprises long-range projections from many different parts of cortex and is the largest fiber bundle in the brain. Previous studies have implicated the corpus callosum in ASD, but studies in young children are lacking.

Objectives: We evaluated the development of the corpus callosum over a two year period from 3-5 years of age in a large sample of children with ASD and age-matched typically developing (TD) controls.

Methods: We acquired structural and diffusion-weighted MRIs in 218 (139 ASD, 79 TD control) children (mean age at baseline 36 months). Longitudinal imaging was carried out annually at two additional timepoints in a subset of this sample (84 with 2 scans, 26 with 3 scans). Specifically, we used (1) structural imaging to evaluate the total size of corpus callosum as well as Witelson subdivisions within the corpus callosum and (2) diffusion tensor tractography to evaluate the organization of callosal fibers based on cortical projection zones as well as the microstructural characteristics of the fibers themselves.

Separate repeated measures models were run for each corpus callosum subsection, with scan year as the repeated measure. Main effects for total cerebral volume, age, gender, and diagnostic group were tested. Interactions between age, gender, and diagnosis were also tested.

Results: Overall, we found that the corpus callosum is smaller in the ASD group than in TD controls, particularly in the rostral body and anterior midbody subsections. Evaluation of change over time revealed that the splenium increased at a faster rate in TD controls than the ASD group.

Evaluation of the organization of the corpus callosum based on cortical projection zone revealed that the region of the corpus callosum containing fibers projecting to the superior frontal cortex is smaller in ASD than in TD controls. In addition, the region containing fibers projecting to orbital frontal cortex increased at a slower rate in ASD relative to TD controls.

When examining the diffusion characteristics of callosal fibers, we found that in children with ASD, fractional anisotropy of fibers projecting to the superior frontal cortex increased at a slower rate, and mean diffusivity and radial diffusivity decreased at a slower rate relative to TD controls. The ASD group also exhibited a faster decrease in mean diffusivity over time in fibers projecting to the orbital frontal cortex than TD controls.

Conclusions: These results suggest that the corpus callosum is developing abnormally in young children with ASD. Specifically, there are abnormalities in the organization of callosal fibers projecting to superior frontal and orbital frontal regions in children with ASD and the fibers themselves are developing on a different trajectory. There are also developmental differences in the splenium that require further investigation. This pattern of results suggests that detailed examination of specific callosal pathways may provide insights into which particular parts of the white matter develop abnormally in ASD.

156.004 Neural Activation to Sentences in Individuals with High-Functioning Autism, Typical Development, and Autism Spectrum Disorder Optimal Outcome. I. M. Eigsti*¹, M. C. Stevens², R. T. Schultz³, L. Naigles¹, E. A. Kelley⁴, A. Orinstein¹, K. E. Tyson¹, E. Troyb¹, M. Barton¹ and D. A. Fein¹, (1)University of Connecticut, (2)Institute of Living, Hartford Hospital / Yale University, (3)Children's Hospital of Philadelphia, (4)Queen's University

Background: Previous functional neuroimaging research has found that youth diagnosed with autism abnormally engage parietal and occipital brain regions associated with visuospatial

processing when reading sentences that do not require imaginative visualization (Kana et al, 2006).

Objectives: The current study used fMRI to compare three groups during processing of sentences that involve low or high levels of visual imagery for reading comprehension: participants with high functioning autism (HFA), typical peers (TD), and individuals with a history of autism spectrum disorder (ASD), but who no longer meet diagnostic criteria for such a disorder (i.e., "optimal outcome" - OO).

Methods: Groups of youth with HFA (n=23), TD (n=21), and OO (n=17) of equivalent mean age (13 years) and gender proportion completed an event-related fMRI task involving Yes/No responses to low-imagery or high-imagery sentences (e.g., "the number six can be rotated to make the number nine").

Brain regions that survived FDR "whole-brain" corrections where high imagery activation was greater than low imagery for all groups (via SPM8 conjunction analysis; $p < .001$ uncorrected) were selected as 5mm radius regions-of-interest (ROIs). Extracted mean data from ten ROIs (left Broca's area, left fusiform, right and left IFG/precentral, right and left IPL/postcentral gyrus, right and left SMA, and right and left posterior MTG) were examined using 2 (high vs low imagery) \times 3 (group) multivariate repeated-measures ANOVA.

Results: Our comparison of high vs low imagery conditions closely replicated previous findings. There was a multivariate effect of group ($p = .001$), but not imagery \times group ($p = .521$). Univariate tests showed that average task activation in left inferior frontal gyrus and supplementary motor area had abnormally high HFA activity; OO activation fell between TD and HFA, and did not significantly differ from TD or HFA. Groups differed in right postcentral/inferior parietal lobule (IPL) and bilateral posterior superior temporal gyrus (BA 37) activation. In the latter regions, TD's either showed no activity or "deactivated" to sentence stimuli, while OO showed abnormally high activation (even greater than HFA hyper-activation). Supplemental analyses found several additional group effects throughout the brain when examining either high imagery or low

imagery conditions. The majority of these differences outside of a priori ROIs occurred near the edges of activated regions, implicating additional ASD abnormality in the extent of activated cortex.

Conclusions: In addition to partially replicating previously reported findings, novel results include the finding that ASD youth with optimal outcomes have partial normalization of abnormal activity observed in HFA, including prefrontal cortex activation in Broca's region and supplementary motor area during sentence comprehension. In addition, OO show exaggerated hyper-activation, greater than both TD and HFA, in posterior brain regions, including those involved with visuospatial processing (right IPL) and object recognition (posterior inferior temporal). The results suggest that during language processing, regardless of visual imagery, activation in the OO group is linked to a mixture of normalization of function in frontal regions and possibly to compensatory over-activation in posterior regions.

156.005 Gender Differences in the Neuroanatomy of Young Children with Autism Spectrum Disorders Detected by Machine Learning Techniques. S. Calderoni^{*1}, A. Retico², A. Giuliano², L. Biagi³, M. Tosetti³ and F. Muratori⁴, (1)*Magnetic Resonance Laboratory, Division of Child Neurology and Psychiatry University of Pisa; Stella Maris Scientific Institute*, (2)*Istituto Nazionale di Fisica Nucleare; Sezione di Pisa*, (3)*Magnetic Resonance Laboratory, Stella Maris Scientific Institute*, (4)*University of Pisa – Stella Maris Scientific Institute*

Background: Genetic, hormonal, and environmental factors contribute since infancy to sexual dimorphism in regional brain structures of typical development subjects. However, the neuroanatomical differences between male and female children with autism spectrum disorders (ASD) are an intriguing and still poorly investigated issue.

Objectives: To evaluate whether the brain regions of children with ASD exhibit sex-related structural differences.

Methods: A total of 152 structural MRI scans were selected. Specifically, 76 ASD children (2-7 years of age; mean=53 months; SD=17) were evaluated employing a support vector machine (SVM) approach to the gray matter (GM) segmented with the SPM8 preprocessing

algorithm, based on the diffeomorphic anatomical registration through exponentiated lie algebra (DARTEL) procedure. The leave-pair-out cross-validation protocol has been adopted to evaluate the classifier performance. The recursive feature elimination (RFE) procedure has been implemented both to reduce the large number of features in the classification problem and to enhance the classifier performance. The SVM-RFE allows also to localize the most discriminant voxels and to visualize them in a discrimination map. Group comparisons consisted of 76 age, gender and non-verbal IQ matched children with typical development or idiopathic developmental delay without autism. In addition, data from 38 male children with ASD and 38 female children with ASD were separately compared with the data of the corresponding age, gender and non-verbal IQ matched control subjects.

Results: SVMs applied to GM scans correctly discriminate ASD male and female individuals with respect to controls with an area under the ROC curve (AUC) above the 87% with a fraction of retained voxels in the 0.4-29% range. By choosing as operative point of the system that corresponding to the lower amount of significant voxels (0.4% of the total number of voxel) we obtained a sensitivity of 0.82 and a specificity of 0.80. The discrimination maps obtained at that operative point showed the following main significant regions where the GM of ASD subjects (males and females) is greater than that of the matched control group: Left (L) and Right (R) Superior Frontal Gyrus (BA 10); L and R Precuneus (BA 31); R Temporo-Parietal Junction (BA 39); L Superior Temporal Gyrus (BA 22); R Superior Temporal Gyrus (BA 41). The separate analysis of the male and female subgroups revealed gender differences in the following regions where an excess of GM is found in the ASD subjects with respect to controls: L and R Precuneus dominates the male ASD group; L and R Superior Frontal Gyrus characterizes both males and females, whereas the Middle Frontal Gyrus prevails in the female group.

Conclusions: Multivariate approach based on the SVM could contribute not only to distinguish ASD from control children, but also to disentangle the gender specificity of ASD brain alterations. Regional neural differences between male and female ASD children could, in its turn, be related

on sex-based differences in the phenotypic expression of ASD disorder. Future studies are therefore warranted to specifically investigate this issue.

156.006 Characterization of Neural Disconnectivity in Autism: A Large-Sample Diffusion Tensor Imaging Study Using Tract-Based Spatial Statistics. J. K. Leung*, C. Cordeaux, S. K. Mitchell, I. Y. Murphy, K. A. Pelphrey and R. J. Jou, *Yale School of Medicine*

Background: Mounting evidence from structural and functional MRI and diffusion tensor imaging (DTI) suggests that the brain phenotype in autism spectrum disorder (ASD) includes deficiencies in long-range neural connections; however, the specific pattern of disconnectivity in ASD is not yet known. Preliminary evidence from our group has implicated the inferior fronto-occipital fasciculus (IFOF) in the pathobiology of ASD, suggesting a potential mechanism for known impairments recognizing emotions in faces.

Objectives: Characterize IFOF and other fiber tract aberrations by comparing a large sample of ASD children to typically developing controls.

Methods: Neuroimaging and behavioral data were collected on 84 participants: 52 children with ASD (age = 8.5 ± 3.5 years) and 32 controls (age = 9.88 ± 3.48 years). Subjects with psychiatric and neurologic disorders associated with ASD were excluded from both groups, and subjects with a history of ASD in first- or second-degree relatives were excluded from the control group. ASD participants had confirmed DSM-IV diagnoses based on expert evaluation using the Autism Diagnostic Interview-Revised and Autism Diagnostic Observation Schedule. To match for cognitive functioning, all subjects completed the Differential Abilities Scale. The Social Responsiveness Scale (SRS) was collected on all subjects to characterize the severity of social disability. Diffusion-weighted MRI (directions = 30 and $b_0 = 5$) were acquired using a 3-Tesla scanner. Fractional anisotropy (FA) was used as the primary measure of fiber tract integrity, which ranges from 0 (low integrity) to 1 (high integrity). Data were analyzed using FMRIB Software Library (FSL). After motion correction, FA maps for all participants were created. Tract-Based Spatial Statistics was used to compare group-averaged FA maps where $p < 0.05$. Affected voxels were labeled using an integrated

white matter tractography atlas. Post-hoc correlation analyses were conducted between mean fiber tract FA and SRS scores.

Results: Of the 84 participants, 17 were excluded due to motion artifact leaving a final sample of 67 (29 controls and 38 ASD). When compared to controls, the ASD group had significant bilateral reductions in FA involving both association and commissure tracts. The most severely affected association tracts included the IFOF and uncinate fasciculus. The most severely affected commissural fibers included the forceps minor. There were neither areas of increased FA in the ASD group nor decreased FA in the control group. There were no significant group differences in intracranial volume, age, race, handedness, and cognitive functioning. All post-hoc correlation analyses involving SRS measures did not reach statistical significance.

Conclusions: This large sample DTI study supports our preliminary data implicating the IFOF in the pathobiology of ASD. In addition, it is consistent with many other studies in the research literature documenting abnormalities in the corpus callosum and uncinate fasciculus. Determining the specific neural phenotype in ASD has implications for more objective diagnosis, targeted intervention, and better understanding of the etiology of ASD.

156.007 The Autism Brain Imaging Data Exchange (ABIDE): Background, Rationale, and Implementation. M. P. Milham*, *Center for Developing Brain at Child Mind Institute*

Background:

The information content of any functional imaging dataset far exceeds what any single investigative group can extract. This insight spurred creation of the fMRI Data Center, which was established to share fMRI data but not embraced by the neuroimaging community. Amid calls for data sharing from research funders, there is also increasing awareness of the problems inherent in underpowered samples: low likelihood of replication and inability to appreciate clinical heterogeneity. While applicable to psychiatric research in general, these challenges are particularly germane to Autism Spectrum Disorders (ASD) – which are marked by complex clinical manifestations and impressive heterogeneity. The recent emergence of resting

state fMRI (R-fMRI) as a mainstream imaging modality has revived momentum towards open data sharing. Over the past four years, the 1000 Functional Connectomes Project (FCP) and the International Data-sharing Initiative (INDI) have pioneered an open neuroscience solution to the challenge of amassing large-scale clinical neuroimaging datasets efficiently. The initial FCP release of 1300+ R-fMRI datasets demonstrated the feasibility and utility of aggregating and openly sharing previously collected neuroimaging datasets for the purposes of comparing findings across sites and carrying out large-scale discovery analyses. More recently, the Attention Deficit Hyperactivity Disorder (ADHD)-200 initiative demonstrated this model could be applied to clinical research to demonstrate unique neural signatures underlying clinical subtypes. Based on the promise and success of this investigator initiated efforts, the **Autism Brain Imaging Data Exchange (ABIDE)** was founded.

Objectives:

To generate and provide a platform for a large-scale R-fMRI and morphometry data aggregation for ASD: ABIDE.

Methods:

Investigators willing to openly share awake R-fMRI data from at least 15 individuals with ASD and 15 matched typical controls were invited to participate in ABIDE. Institutional IRB approval or waiver was required prior to data contribution. Basic phenotypic measures that are standard in the ASD field (e.g., age at scan, sex, IQ, DSM-IV TR diagnosis, ADOS and ADI-R scores) were also aggregated for analyses and sample characterization. Scripts for full anonymization and a pipeline for data integrity checking and aggregation were developed. ABIDE data aggregation was based on the INDI platform.

Results:

Twenty previously collected autism brain imaging samples were received from 16 independent imaging sites, yielding a total of 1112 datasets (from ages 7 to 64). Following data upload, aggregation, organization, and verification, we publically released the ABIDE dataset on Aug 30,

2012 via www.nitrc.org at (http://fcon_1000.projects.nitrc.org/indi/abide/).

Conclusions:

The FCP/INDI model was successfully extended to the autism field. Similar to the initial FCP dataset which has yielded more than 40 publications since 2010, and the ADHD-200 release which has yielded 12 publications in the last year, we expect to witness a rapid proliferation of manuscripts examining the neural correlates of ASD using the large-scale ABIDE dataset. The ABIDE dataset will not only allow the testing and generation of hypotheses using an adequately powered imaging dataset, but facilitate the exploration of neural and clinical subtypes and the potentially confounding effects of variables such as those related to IQ.

Treatment Trials: Behavioral Interventions Program

157 Treatments: Behavioral Interventions

This session includes large controlled and/or novel behavioral trials.

157.001 Comparative Effectiveness Trial of School and Home-Based Executive Functioning Versus Social Skills Intervention for Children with Asd; Part 2: Performance-Based Effects. L. Kenworthy*¹, M. A. Werner², K. C. Alexander², J. F. Strang¹, M. Wills¹, C. Luong-Tran¹, J. L. Sokoloff¹, E. Bal¹, L. Cannon², A. C. Sharber¹, M. Rosenthal³, G. L. Wallace⁴ and L. G. Anthony¹, (1)*Children's National Medical Center*, (2)*Ivymount School*, (3)*Child Mind Institute*, (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.

Objectives: To evaluate the effectiveness of UOT as compared to a social skills intervention (SS) of equal intensity, and as implemented in mainstream elementary schools.

Methods:

The interventions occurred in 14 mainstream elementary schools. All children had IQ>70 (mean=108), met criteria for ASD on ADOS or ADI and clinician impression, and were in 3rd-5th grade. Forty-seven (87% male) children received UOT, and 20 children (90% male) received SS. The groups were well-matched at the start of the intervention for age, type of school, parent education, IQ, % minority, and % on psychotropic medication. Comparable proportions of participants completed the intervention (91% of UOT and 95% of SS). Both interventions were delivered during the school day by school staff in small groups; classroom teachers and parents were trained to reinforce the UOT or SS lessons. The two interventions were matched for dose of intervention with the child, and on amount of parent, teacher and group leader training. Fidelity was measured through observation of intervention groups and pre-post change was measured through contextual data collection and laboratory measures, specifically the Wechsler Abbreviated Scale of Intelligence Block Design (BD) subtest, and an ADOS-like interview designed to measure EF, The Challenge Task (CT). The CT challenges children to be flexible and to plan in the context of activities with an examiner (e.g., doing a puzzle), and yields Flexibility and Planning scores, as well as a rating of Social Appropriateness. Evaluators were blind to intervention type. Pre- post-data were compared through repeated measures ANOVA, with intervention group as the between subjects factor.

Results:

See companion IMFAR abstract for findings regarding fidelity and contextual data. There was a significant group (UOT, SS) by time (pre-, post-intervention) interaction for BD ($F=4.82, p<0.03$) and CT Flexibility ($F=6.89, p<0.01$) scores; post-hoc paired sample t tests showed a significant improvement in BD and CT flexibility scores for the UOT group (BD $t=-2.81, p<0.01$; CT Flex $t=-7.30, p<.001$) but not the SS group. In contrast, there were significant overall time effects indicating that both UOT and SS CT Planning and Social Appropriateness scores improved (CT Plan: $F=24.36, p<0.001$; CT Social: $F=5.22, p<0.03$).

Conclusions: These data indicate that UOT improves flexibility and efficiency of problem solving in children with ASD. The benefits of UOT are significant even when compared to a social skills intervention of equal intensity. The fact that this intervention was successfully implemented in mainstream educational settings by individuals with variable background and training in ASD, provides further indication that UOT can be a useful tool for improving executive and social skills in children with ASD.

157.002 Moderators of a Theory of Mind Intervention for Children with Autism Spectrum Disorder: A Randomized Controlled Trial. S. Begeer*¹, E. Hoddenbach¹, P. Clifford², C. Gevers², C. Clauser³, F. Boer⁴ and H. M. Koot⁵, (1)VU University Amsterdam, (2)Wei43, (3)De Bascule, (4)University of Amsterdam, (5)VU University

Background:

Theory of Mind, the ability to attribute mental states to oneself or others, is a central domain of impairment among children with an Autism Spectrum Disorder (ASD). Many interventions focus on improving Theory of Mind skills in children with ASD. Nonetheless, the empirical evidence for the effect of these interventions is limited. Moreover, treatment outcomes appear to vary among children with ASD.

Objectives:

The main goal of this study was to examine the effectiveness of a short Theory of Mind intervention in a large group of children with ASD. A second objective was to determine whether the treatment outcome was moderated by social interaction style (Scheeren, Koot & Begeer, in press), and co-morbid problem behavior.

Methods:

One hundred children with ASD and a normal IQ, aged 7 to 12 years, were randomly assigned to an intervention- or a waitlist control group. Outcome measures included a battery of Theory of Mind tasks (Muris et al., 1999) and emotion understanding tasks (LEAS-C, Bajgar et al., 2005), and parent- and teacher questionnaires on children's social skills (SRS, Constantino & Gruber, 1997; SSQ, Spence et al., 2000). Follow up data for the intervention group were collected

6 months after the interventions. Moderator variables included social interaction style, based on the Wing Subgroups Questionnaire (Castelloe & Dawson, 1993; Scheeren, et al., in press), and co-morbid problem, based on the Disruptive Behavior Disorders rating scale (Pelham et al., 1992).

Results:

Preliminary analyses on 80 of the 100 participants indicated positive effects of the intervention on the primary outcome measures. Children in the treatment group improved significantly compared to the waitlist control group in their performance on Theory of Mind and emotion understanding tasks. Moreover, parents and teachers reported enhanced social skills in children's daily life functioning. The effects on social skills were moderated by social interaction style and co-morbid problem behavior. In particular, children with a passive social interaction style or higher levels of problem behavior showed lower treatment benefit.

Conclusions:

The current findings are promising with regard to the effectiveness and generalization of a short intervention focused on Theory of Mind skills. However, the moderator effects indicate systematic individual differences in treatment outcomes. A passive social interaction style and co-morbid problem behavior were shown to hamper the effect of the treatment. These findings highlight the need for treatments targeting specific social skills in specific groups of children with ASD.

157.003 One Size Doesn't Fit All - A Randomized Comparison of Intensive Imitation Versus Treatment As Usual. M. Heimann^{*1}, B. Spjut Janson² and T. Tjus². (1)*The Swedish Institute for Disability Research*, (2)*University of Gothenburg*

Background: Although imitation is viewed as a core deficit in autism by many researchers and clinicians, a contrasting view holds that it is not imitation in itself that is the problem. Rather, a primary social motivation deficit explains the low levels of imitation usually observed among children with autism. According to this latter view, Intensive Imitation (that is, the adult imitates everything the child does; see Nadel et al, 2000)

can create an awareness of the other person, a social interest. Several studies have explored this idea and the findings tend to confirm the hypothesis (e.g.: Escalona et al., 2002; Heimann et al., 2006): Intensive Imitation increases the social awareness in young children with autism, especially in children with no or very low language levels. Based on these findings it has been proposed that repeated sessions of imitation might be an additional intervention strategy for young children with autism.

Objectives: To investigate how young children with autism respond to Intensive Imitation (II) compared to treatment as usual when given as the first intervention after receiving an autism diagnosis. It is well known that the treatment as usual method, Intensive Behavior Therapy (IBT), is effective. Thus, the main goal of the study was not to see which one of the method that is better, but to gain information that can help us tailor treatment to the individual child. Children with autism are a heterogeneous group that to a high degree responds differently to various intervention methods.

Methods: Forty families with children that have been newly diagnosed with autism were invited to the study. The children were randomized to one of two 12-week long interventions: Intensive imitation (II) or Intensive Behavior Therapy (IBT). To date, 36 children have completed the intervention (29 boys, 7 girls), 19 have received II and 17 IBT. The intervention started on average two months after receiving the diagnosis when the children were around 3:6 years old. Based on the Bayley the two groups did not differ in mental age. The children were evaluated with an extensive battery (e.g.: PEP, ESCS, Bayley, imitation, memory, video observations of social interaction) at start, end, and at a follow-up one year later.

Results: Although children in both groups show progress, the children in the II group tend to change their communicative style to a higher degree. They also became more positive towards physical closeness and increased their eye contact. There is also some indication that II promotes language development and joint attention albeit this is not finally analyzed yet. In addition, the preschool teachers being involved in

the project describes II as an attractive method that is relatively easy to learn.

Conclusions: As expected, both methods promote development. II has the advantage of being relatively easy to learn and that it does not involve the parents to the same degree as IBT. Thus, II might be an important complement to the more 'traditional' behaviorally based methods that we know are effective but are also very time costly.

157.005 Early Social Interaction Project for Toddlers with Autism Spectrum: Effects On Social Communication, Developmental Level, Adaptive Behavior, and Autism Symptoms. A. M. M. Wetherby^{*1}, J. J. Woods¹, W. Guthrie², C. Schatschneider², R. Holland¹, L. Morgan¹ and C. Lord³, (1)Florida State University Autism Institute, (2)Florida State University, (3>Weill Cornell Medical College

Background: The AAP recommends that all children be screened for ASD at 18-24 months, making the need for evidence-based interventions for toddlers with ASD a priority. The Early Social Interaction Project (ESI) is a parent-implemented intervention that is a cost-effective approach to achieve the intensity needed for toddlers with ASD by teaching parents to embed naturalistic behavioral strategies within everyday activities.

Objectives: The major objective of this randomized controlled trial was to compare two parent intervention conditions for 9 months: 1) a parent-implemented intervention (PII) offered in 3 weekly sessions for 6 months and 2 weekly sessions for 3 months to teach parents how to embed strategies to support social communication skills for 25 hours a week within everyday activities; and 2) an information, education and support group (IES) offered weekly.

Methods: A crossover design was used with all dyads receiving 9 months of each condition. Pairs of children matched on pretreatment nonverbal developmental level were randomly assigned to first treatment condition. The effects of initial treatment condition for 82 children with ASD enrolled at 18-20 months are reported. Effectiveness of PII and IES was compared on measures of social communication (CSBS), developmental level (Mullen), adaptive behavior (Vineland), and autism symptoms (ADOS).

Results: Comparisons indicated baseline equivalency of condition groups on all outcome variables. After 9 months of intervention, children in both conditions showed significant improvement on all 3 composites and 7 clusters of the CSBS but children in PII made significantly greater gains than IES on the social composite (timeXcondition: $F(69)=7.00, p=.01$) and the communication cluster ($F(69)=8.12, p=.006$), with a trend toward greater gains for the PII group on the emotion and words clusters ($F(69)=3.75, p=.057$; $F(69)=3.31, p=.073$). On the Mullen, children in both conditions showed significant improvements in T-scores on receptive and expressive language scales but children in PII showed significantly greater gains in receptive language ($F(68)=5.49, p=.02$). Children in both conditions showed no significant change in visual reception but showed a significant decrease in fine motor. On the Vineland, children in both conditions showed significant improvements in communication but children in PII showed significantly greater gains ($F(68)=4.97, p=.03$). Children in PII showed no significant change in social but children in IES showed a significant decrease ($F(32)=5.93, p=.02$). Children in both conditions showed no significant change in daily living and showed a significant decrease in motor. On the ADOS, children in both conditions showed a significant decrease in symptom severity on social affect and no significant change in restricted, repetitive behavior.

Conclusions: Taken together these findings support the effectiveness of ESI, a cost-effective, community-viable intervention. Children in both conditions showed significant improvements on social communication and language but PII demonstrated significantly greater efficacy on some measures of social communication and receptive language. These findings are particularly important in light of the lack of main effects of other parent-implemented interventions for toddlers. These findings will be discussed in relation to other parent- and clinician-implemented interventions, with consideration to how autism can worsen in this time period without intensive intervention.

157.006 Enhancing Mothers' Interactions with Toddlers. N. Jaegermann^{*1} and P. S. Klein², (1)Bar-Ilan University, Israel, (2)Bar Ilan University, Israel

Background:

Sensory processing is defined as the ability to receive sensory information from the environment and the body and to respond appropriately. Self-regulation refers to the capacity to control the nature and the intensity of one's responses. In the current study, the term Sensory Processing Disorders (SPD) refers to toddlers with both sensory-processing and self-regulation difficulties.

Numerous studies have shown that primary symptoms of SPD predict developmental difficulties at an older age. SPD often occur prior to the diagnosis of autism and may be one of the first signs that a child is at risk and in need of referral for assessment and possible intervention. Thus, early identification and intervention are most important with toddlers who exhibit early signs of SPD.

Objectives:

The objective of the current study was to examine the effects of a brief (6-8 weekly sessions) Mediation Intervention for Sensitizing Caregivers (the MISC-SP) designed to enhance the quality of mothers' interactions with their toddlers who have SPD. The MISC-SP intervention had two main objectives: 1. To help each mother understand the constitutional origin of her toddler's challenging behavior and to enhance her ability to promote her child's self-regulation and adaptive behavior by adapting her own behavior to her child's special sensory and regulatory needs. 2. To promote each mother's interactive behavior by enhancing her awareness of general criteria for quality parent-child interaction.

Methods:

The effects of the intervention were compared to those of another intervention that was based on the Sensory Integration approach (SI) designed to enhance children's sensory functioning and to a control group receiving no intervention during the study. Participants were 86 toddlers (12-18 months old) with early signs of SPD and their mothers, who were randomly assigned to the aforementioned three research groups. The SI intervention was held during 8 weekly sessions. Both interventions were carried out by four Occupational Therapists who were especially trained in both intervention approaches.

Results:

Following the intervention, toddlers in the MISC-SP group improved on measures of motor behavior, communicative behavior, and responses to vestibular sensory stimulus. Toddlers in the SI group improved their communicative behavior, but significantly less than the MISC-SP group. Control group toddlers did not show improvement on any of the adaptive-developmental functioning measures. Hierarchical regression analysis revealed that the change in mothers' behavior toward their children following the intervention explained a significant amount of the variance in toddlers' motor behavior improvements, as well as a significant amount of the variance in toddlers' improvement in interactional communication abilities.

Conclusions:

This study demonstrated that a short-term intervention program, which targeted the quality of interactions between mothers and their toddlers with SPD, brought about an improvement in children's adaptive-developmental functioning. These outcomes support the assumption that improving mother-child interaction renders a significant effect on specific behaviors of toddlers who reveal early signs of SPD, including behaviors essential for developing self-regulation and communication abilities.

157.007 Randomized Controlled Trial of Pivotal Response Treatment (PRT) Parent Training Group. G. W. Gengoux^{*1}, M. B. Minjarez², K. L. Berquist³, J. M. Phillips³, T. W. Frazier⁴ and A. Y. Hardan⁵, (1)Stanford University School of Medicine/Lucile Packard Children's Hospital, (2)Seattle Children's Hospital, (3)Stanford University, (4)Cleveland Clinic Lerner College of Medicine, (5)Stanford University School of Medicine

Background: As rates of autism spectrum disorder have increased in recent years, the need for effective and efficient service delivery models continues to expand. In previous studies of Pivotal Response Treatment (PRT), research has documented that parents can learn this evidence-based treatment using a family therapy model; however, few studies have looked at more efficient service delivery models, such as group treatment. Previous pilot studies have supported the use of a group therapy model, but no

randomized controlled trials have been completed to date.

Objectives: The current investigation is a randomized controlled 12-week trial, examining the efficacy of Pivotal Response Treatment Group (PRTG) in targeting language deficits in young children with autism. This condition is compared to parents participating in a psychoeducational group (PEG). The research hypothesis is that parents participating in PRTG will demonstrate evidence of more targeted PRT skills and that their children will show significant benefits in language abilities, relative to those in the PEG.

Methods: Participants included children (age range: 2-6.11 years) with autism and significant language delay. Children were randomized into either the PRTG or PEG. The PRTG taught parents PRT to facilitate language development. The PEG addressed general topics related to the assessment and treatment of autism. Video-taped assessments (structured lab observation of parent-child interactions) and standardized measures (e.g., Vineland-II) were conducted at baseline, week 6, post-treatment, and three month follow-up and were rated by a blind investigator.

Results: Fifty-three participants were randomized to either PRTG (N=27) or PEG (N=26). Preliminary analyses suggest that group parent education is an effective method for teaching parents to implement PRT with their children and that a majority of parents (approximately 83%) in the PRTG met PRT fidelity of implementation criteria after 12 weeks of treatment. Analysis of changes in child communication for families who completed the trial (PRTG N=26; PEG N=20) revealed that children whose parents participated in the PRTG exhibited a significant increase in the number of utterances (23.08 ± 22.97) compared to those whose parents participated in the PEG (8.65 ± 22.20 ; $t = -2.14$; $df = 44$; $p = 0.038$). Changes on a standardized measure of adaptive communication were also observed following PRTG. Specifically, children whose parents participated in the PRTG showed greater improvement on the Vineland-II compared to children whose parents participated in the PEG on the Receptive Communication V-Scale score (PRTG: 1.29 ± 2.03 ; PEG: 0.06 ± 1.77 ; $t = -2.062$; $df = 40$; $p = 0.046$) and the overall

Communication Standard Score (PRTG: 6.13 ± 7.94 ; PEG: 0.83 ± 8.54 ; $t = -2.069$; $df = 40$; $p = 0.045$). Changes on the Expressive Communication V-Scale score approached significance (PRTG: 0.71 ± 1.20 ; PEG: -0.32 ± 2.187 ; $t = -1.957$; $df = 41$; $p = 0.057$).

Conclusions: These findings suggest that, compared with general parent psychoeducation sessions, specific instruction in PRT results in greater skill acquisition for both parents and children. These findings provide preliminary evidence supporting the usefulness of PRT in targeting language deficits in children with autism and warrant larger trials to attempt to replicate these findings and potentially identify predictors and mediators of response.

157.008 Telehealth Delivery of Cognitive-Behavioral Intervention for RURAL YOUTH with ASD and Anxiety: Feasibility and Preliminary Efficacy. S. Hepburn^{*1}, J. Reaven² and A. Blakeley-Smith³, (1)University of Colorado/JFK Partners, (2)JFK Partners/University of Colorado School of Medicine, (3)University of Colorado School of Medicine/JFK Partners

Background:

Youth with Autism Spectrum Disorders (ASD) are underserved in several aspects of health care, including mental health services (Mandell et al, 2005). Reports of psychiatric comorbidity are high and symptoms are significantly impairing (de Bruin, Ferdinand, Meester, de Nijs, & Verheij, 2007). Finding innovative ways to provide evidence-based interventions to families who live far from specialty medical centers is an important goal for translational research.

Objectives:

This is a phase-II, quasi-experimental study of the clinical viability of delivering cognitive-behavioral intervention through videoconferencing to youth with ASD and clinically significant anxiety symptoms. The purpose of the current study was to examine the 1) acceptability, 2) feasibility and 3) preliminary efficacy of an evidence-based, family-focused intervention (i.e., *Facing Your Fears* (FYF; Reaven et al, 2011) to psychiatrically complex youth in rural Colorado through OoVoo, a commercially available videoconferencing application.

Methods: Twenty parent/child pairs from rural Colorado met inclusion criteria for the study (e.g., confirmed diagnosis of autism and clinically significant symptoms of anxiety) and participated in 10 sessions of "Facing Your Fears" delivered through the internet in either 1-family, 2-family, or 4-family groups. *Acceptability* was measured through parent and youth report on a satisfaction questionnaire. *Feasibility* was assessed through a multi-method strategy, including monitoring intervention completion, session attendance, technical difficulties, and adherence to the key elements of FYF. Preliminary estimates of efficacy were obtained through youth and parent report of anxiety symptoms (SCARED; Birmaher et al, 2002), fears (Fears Survey Schedule for Children-II; Gullone & King, 1992) and parent report of family functioning (Family Impact Questionnaire, Donenberg & Baker, 1993) at pre-treatment, post-treatment and 3-month follow-up.

Results: *Acceptability*. Satisfaction was rated as "very high" for 95% of parents, 72% of school-aged children, and 50% of teens. *Feasibility*. Eighteen of 20 families completed the intervention and all 18 families completing the treatment attended 85% of sessions or more. There was a 70% chance of technical difficulties in the first 3 sessions and a 30% chance in subsequent sessions. Fidelity of telehealth delivery to the key elements of the FYF intervention was strong for the psychoeducational component, but less robust for sessions focused on graded exposure activities. *Efficacy*. Pre- vs. post-treatment data are available for analysis, with follow-up data to be provided. Effect sizes for youth and parent report of anxiety symptoms were .39 and .04, respectively; with greater impact noted on youth and parent report of specific fears (effect sizes of .82 and .24, respectively). Parents reported a significant improvement in the youth's impact on the family's overall functioning (Cohen's $d = 1.28$).

Conclusions: Telehealth delivery of the manualized mental health intervention was feasible and acceptable to families, but challenging for therapists. With modifications, telehealth platforms may improve access to potentially therapeutic, direct intervention with clinicians. More work is needed to improve delivery of some program components. Results must be interpreted with caution, due to the

quasi-experimental design (no comparison group) and reliance on non-independent observers. The next step is to conduct more rigorous efficacy studies of telehealth delivery.

Cognition and Behavior Program

158 Cognition and Behavior

158.001 1 Eye-Tracking Study Investigating Performance Differences Between ASD and Non-ASD Groups in Simple and Complex Emotion Recognition Tasks. J. Adachi*, *Hokkaido University of Education*

Background: Individuals with Autism Spectrum Disorders (ASD) have a difficulty of emotion recognition. The performance is worse with complex emotions than simple emotions (Golan et al., 2006).

Objectives: The-eye tracking study was designed to investigate the influence of task complexity on the performance differences between ASD and non-ASD groups in simple and complex emotion recognition tasks.

Methods: The participants were 25 adults (12 with ASD and 13 without ASD) with normal IQ. The twenty-seven movie stimuli were constructed (three semantically neutral sentences in each of three vocal emotions with each of three facial emotions). Three emotions were happy, angry and sad. The nine stimuli were congruent and the eighteen stimuli were incongruent between the facial emotion and the vocal emotion. The participants were given two simple tasks and two complex tasks. The two simple tasks were the auditory task and the visual task. The auditory task was to recognize vocal emotion in each of the movie stimuli with audio-only presentation. The visual task was to recognize facial emotion in each of the movie stimuli with video-only presentation. The two complex tasks were the emotion labeling task and the congruent-incongruent task. The emotion labeling task was to label one of three emotions to each of the movie stimuli. The congruent-incongruent task was to judge whether the facial emotion and the vocal emotion in each of the movie stimuli were congruent or not. Three measurements were used: percentage of correct responses, mean reaction time and fixation behavior. In the emotion labeling task, percentage of correct responses was not recorded because the task has no correct answers except the congruent movie stimuli. In the auditory task, fixation

behavior was not recorded because no video was presented in the task. The Tobii 1750 eye-tracker system was used to record eye movements and analyze the fixation behavior.

Results: The percentage of correct responses in the congruent-incongruent task was significantly higher in the non-ASD group than in the ASD group. In the auditory and the visual tasks, the two groups were not significantly different. The mean reaction times in both the auditory and the visual tasks were longer in the ASD group than in the non-ASD group. In the emotion labeling and the congruent-incongruent tasks, the two groups were not significantly different. The fixation behaviors in both the emotion labeling and the congruent-incongruent tasks were significantly different between the two groups. In both tasks, the ASD group fixated significantly more in the mouth region and significantly less in the eye region than the non-ASD group. In the visual task, the two groups were not significantly different.

Conclusions: The findings suggested as follows: the ASD group (1) performed as well as the non-ASD group but needed more time to recognize emotion in the simple emotion recognition task with a single modality, (2) performed worse and changed their fixation behavior in the multi-modal complex emotion recognition task.

158.002 2 A-ToM: A New Measure of Theory of Mind in Adults. N. Brewer* and R. L. Young, *Flinders University*

Background: A Theory of Mind (ToM) deficit suggests an inability to explain, predict, empathise with and understand behaviours, intents and emotions of others. Although ToM is believed to be delayed or deficient in children with ASD, adult data highlight considerable variability in the degree of deficit (Baron-Cohen, 2001). One of the most widely used ToM tests is Happé's Strange Stories test (Happé, 1994). The original set of items comprised 24 pencil-and-paper vignettes about everyday situations that require participants to identify motivations that may underpin utterances that are not literally true. These vignettes require participants to recognise expressions of sarcasm, a white lie, a figure of speech, and so on. It has been argued, however, that the variability in ToM performance among adults with ASD results from such measurement tools allowing adults to "hack out" a strategy that

provides an appropriate response (Frith et al., 1991) rather than indicating ToM variability per se.

Objectives: In line with this proposition, we developed a tool that does not allow participants time to apply analytic reasoning skills to determine the appropriate response. This tool (Adult Theory of Mind: A-ToM) comprises acted-out "strange stories" (i.e., films) from Happé's test using visual and auditory contextual cues to assess ToM. The A-ToM simulates real life situations in which people are required to make decisions based on ambiguous social cues and subtle social information presented in a short film. We also examined the psychometric properties of this measurement tool.

Methods: Participants viewed films based on Happé's (1994) Strange Story tasks and were required to provide a written response to the question associated with each script within one minute. Participants were required to interpret the events in the films as they unfolded, just as they would in real life (cf. having an opportunity to read, reread, and think about the story as can happen with a pencil-and-paper scenario), thereby limiting the opportunity for "hacking out" correct responses. We examined internal consistency, and test-retest reliability after a 2 week interval. Concurrent validation was investigated by correlating A-ToM performance with performance on Happé's Strange Stories Test, and the Reading the Minds in Films (Golan, Baron-Cohen, Hill & Golan, 2006) for a sample of (i) non-ASD adults ($N = 100$) and (ii) individuals with an ASD ($N = 50$).

Results: The final version included only those items characterised by reasonable internal consistency and test-retest stability. The validity of the instrument was suggested by the following pattern of findings: (i) the correlation between A-ToM performance and performance on Happé's Strange Stories and the Reading the Minds in Films tests. (ii) the different performance levels for the A-ToM compared with existing pencil-and-paper ToM scales. (iii) performance differences between ASD and non-ASD participants on the social versus physical items.

Conclusions: This study introduces a psychometrically sound tool for assessing ToM

among adults with ASD. The tool involves a naturalistic setting and demands real-time responsiveness, reducing the capacity for participants to “hack out” solutions.

158.003 3 Meta-Analysis of Imitation Abilities in Children with Autism Spectrum Disorders. L. A. Edwards*¹ and C. A. Nelson², (1)*Harvard University, Boston Children's Hospital*, (2)*Boston Children's Hospital*

Background: Imitation is essential for social and cognitive learning and typically arises early in development. Mixed results on the imitative abilities of children with autism spectrum disorders (ASD) and other developmental disorders demonstrate that it is not yet clear whether impairments in imitation are significant and specific to the condition of having ASD. Although several systematic reviews of imitation in autism (see Rogers, 1999, 2006; Smith & Bryson, 1994; Vanvuchelen, Roeyers & De Weerd, 2011), and most recently a quantitative review of action imitation in ASD (Williams, Whiten & Singh, 2004) exist, this meta-analysis will serve to update prior reviews and is the first known meta-analysis to quantitatively synthesize studies on facial/emotional, body, and object-oriented imitation.

Objectives: In this metanalytic study we seek to determine whether children with ASD show significant imitation deficits in comparison to typically developing children (TD), and children with non-ASD developmental disorders (DD). The current study also reports on the magnitude of any differences in imitative abilities found, and whether these are specific to children with ASD.

Methods: An extensive literature search was conducted to identify studies relevant to the current analysis. Those studies that directly assessed imitative abilities, tested children with non-syndromic ASD, and contained at least one control group were included in the final analysis. Participants ranged in age from 20.3 months to 18.5 years. Using standard meta-analytic techniques in a random-effects model, performance on imitation tasks by children with ASD was compared to that of TD and DD children. Subgroup analyses were also conducted to assess the impact of study setting and imitation task type on the relative performance of these three groups.

Results: Preliminary results from a 10 percent random probability sample of the included studies ($n_{\text{studies}}=9$; $n_{\text{subjects}}=153$ ASD, 154 TD, 157 DD) suggest that children with ASD show deficits in imitation, performing on average 1.28 SDs below children without ASD on general (facial, body and object-oriented imitation) tests. Imitation deficits did not vary by age, and were specific to ASD, rather than a general feature of developmental delay. A mixed-effects moderator analysis of the effect of study setting on imitation in ASD suggests however, that imitation deficits are only observed in studies carried out in unfamiliar settings; studies that were conducted in familiar environments found that children with ASD imitated comparably to children without ASD.

Conclusions: The generalizability of these results is limited, as the studies included in this analysis are a small subsample of the larger population of studies on imitation in ASD. Nonetheless, these findings suggest that impairments in imitation abilities found in laboratory studies are significant and specific to the condition of having ASD. The observed impact of study setting on the imitative deficits of children with ASD have important implications for the validity of studies of children with ASD, and they may call for a move to more familiar—rather than laboratory-based—study environments.

158.004 4 Prevalence of Neuro-Developmental Disorders in India. V. B. Deshmukh*¹, A. Mohapatra¹, S. Gulati², M. Nair³, V. K. Bhutani⁴, D. H. Silberberg⁵, N. K. Arora¹ and I. Group⁶, (1)*The INCLEN Trust International*, (2)*All India Institute of Medical Sciences*, (3)*Medical College*, (4)*Stanford University School of Medicine and Lucile Packard Children's Hospital*, (5)*University of Pennsylvania Medical Center*, (6)*The INCLEN NDD Study Group, The INCLEN Trust International*

Background: Due to lack of awareness of neurodevelopmental disorders (NDDs) and resources for diagnosis and provision of services among parents as well as health care providers and educators, many children with NDDs in India remain undetected and thus untreated. . Also the services available are grossly inadequate and inappropriate as per the anticipated requirement. As noted in the 2008 UNICEF report on child disability in developing countries, clinical diagnostic evaluations for children at risk for disability are essential to developing treatment programs and other intervention programs. The current project was undertaken to address these

issues and to provide an enabling environment for children with one or more of these NDDs.

Objectives: To assess the prevalence of ten (10) common neuro-developmental disorders (NDDs) among children aged 2-9 years in India.

Methods: The prevalence was estimated using Consensus Clinical Criteria (CCC). The CCCs had been identified/ prepared and validated for diagnosing the NDDs based on universally accepted criteria like DSM IV-TR, ICD-10 and WHO. Population proportionate to size (PPS) cluster sampling technique covering 4000 children across five geographic populations at five sites in India viz [Palwal (Haryana); Kangra (HP); Hyderabad (AP); Denkanal (Orissa) and Goa (Goa)] (50 clusters in three states & 25 clusters in two states) was employed to recruit participants. Firstly, the screening tool (NDST) was applied, separately by a doctor and by social scientist, on 20 children per cluster (10 each from the 24-71 months and 72-107 months with equal number of boys and girls in each category) at their residence on two consecutive days. Following this, all these children were mobilized to a health facility for administration of the diagnostic consensus clinical criteria by a team of doctors, clinical psychologist and audiologist.

Results: The application of the CCC shall yield the overall prevalence NDDs and specific disorders. The prevalence of all nine NDD (excluding HI) in 2-5 yrs of children is 11.2 % [95% CI=0.08-14.0] and in 6-9 yrs of children is 15.2% [95% CI=12.3-18.7]. The preliminary data from one site shows 0.9% [95% CI=0.04-1.7] prevalence for ASD. Of the children who were identified as having NDD, 78.2 % [95% CI=71.5-83] had single NDD and 20.6% [95% CI=15.3-27.2] exhibited more than one NDD in 2-9 years of children (preliminary data). The analysis is ongoing and detailed result for behavioral, neurological and sensory disorders from all the sites would be presented, both an aggregate and separately.

Conclusions: The preliminary results highlight the concerning magnitude of NDDs across the country. This call for concerted policy making for appropriate resource allocation and targeted rehabilitative interventions so that these children could be brought to mainstream society without

stigmatization help them achieve their maximal potential.

158.005 5 Importance of Group Intervention On ASD-Generalization of Social Skills. A. Ana Aguiar¹ and A. Mira Coelho*²,
(1)Centro de Educação e Terapia, (2)Pediatric/Psychiatric Department Hospital S.Joao

Background:

Autism Spectrum Disorders (ASD) consists in a complex and diverse development disorder. In recognition of generalization difficulties as fundamental deficit, along the autism spectrum and social comprehension problems, it seemed essential to develop an intervention program aimed to promoting not only the acquisition but also the generalization of social skills associated with Theory of Mind (ToM). One of the aspects for generalization to occur, is to promote social understanding through group therapeutic approaches.

Objectives: We wanted to test whether social skills acquired could be generalized. Having been used an intervention Group, which conducted the completed intervention program, and a comparison group which held just a phase of acquisition, expecting that first Group were able to generalize and to adapt the skills of ToM acquiring new contexts.

Methods: The initial sample included a total of 12 children with Asperger Syndrome (6 belonging to the intervention Group-G1 and 6 in the comparison Group-G2). Age of the children between 74 and 91 months (M = 82.42; DP = 4.85). **INSTRUMENTS:** *Diagnostic Criteria Instruments (Gillberg and Gillberg); Vineland Adaptive Behavior Scales; Australian Scale for Asperger's syndrome evaluation; Tests of theory of mind (ToM).* **PROCEDURE:** The 6 children who constituted the G1 frequented an individual support session and a session of group social skills training. Children of the G2 were matched with children of G1 in terms of age, year of schooling, Intellectual Quotient and number of symptoms. Three evaluation moments occurred (M1, M2, M3), final assessment was when G1 concluded the generalization phase and G2 concluded the acquisition phase.: To make the comparison between G1 and G2, we brought out the Kruskal-Wallis test, the non-parametric test equivalent to one-way ANOVA independent.

Firstly, we proceeded to the comparison between the two groups for each of the assessment moments

Results: About the characteristics of Asperger Syndrome, evaluated by EASA, exists a significant difference between the G1 and G2. Specifically we can say that in M2, the G1 has a domain of ToM ($H(1) = 11.00$, $p < .001$). The test results show a significant trend Jonckheere towards a higher domain of ToM by G1 in M2, $J = 0$, $z = -3.32$, $r = -.96$. Also in M3, the G1 has a domain of ToM ($H(1) = 5.6205$, $p < .$). The test revealed a significant trend in Jonckheere results towards a higher domain of ToM by G1 in M3, $J = -2.37$, $z = 4$, $r = -.68$.

Conclusions: The analysis of results seems to confirm the initial hypothesis of this study. There was a gradual evolution of the two groups but this development was significantly higher in the case of the intervention group, just after the period of generalization. The results pointed toward the possibility of social skills acquired may be generalized on the basis of a structured, systematic and intensive intervention.

Genetic Factors in ASD Program

159 Epigenetics and Gene-Environment Interaction

159.006 6 Complex Epigenetic Regulation of Engrailed-2 (EN-2) Homeobox Transcription Factor Gene in the Autism Cerebellum. S. J. James^{*1}, S. Shpileva², S. Melnyk¹, O. Pavliv¹ and I. P. Pogribny², (1)University of Arkansas for Medical Sciences, (2)National Center for Toxicological Research

Background: The *EN-2* homeobox gene is considered to be an autism susceptibility gene based on neuroanatomical parallels between autism and cerebellar developmental abnormalities in rodent models and also on family linkage studies indicating an over-transmission of *EN-2* polymorphic variants from parents to affected children. The normal timing of Purkinje cell maturation and cerebellar patterning is critically dependent on perinatal *EN-2* down-regulation, which is disrupted with *EN-2* overexpression.

Objectives: The elucidation of epigenetic alterations in the autism brain has the potential to provide new insights into the molecular mechanisms underlying abnormal gene expression

associated with this disorder. Given strong evidence that *EN-2* is a developmentally expressed gene relevant to cerebellar abnormalities and autism, the epigenetic evaluation of this gene was undertaken.

Methods: Frozen cerebellar samples from 26 case and control post mortem cerebellar samples were matched for age, gender, PMI, race, and cause of death. Assessments included genome-wide DNA methylation, *EN-2* promoter methylation, *EN-2* gene expression and protein levels. In addition, chromatin immunoprecipitation methodology was used to evaluate trimethylation status of histone H3 lysine 4 (H3K4) associated with gene over-expression and H3 lysine 27 (H3K27) associated with gene down-regulation. The binding of GATA-1, an enhancer element with binding motifs in the *EN-2* promoter, was also evaluated.

Results: The results revealed an unusual pattern of global and *EN-2* promoter DNA hypermethylation that was accompanied by an increase in *EN-2* gene expression and protein levels. Consistent with *EN-2* over-expression, histone H3K27 trimethylation mark in the *EN-2* promoter was significantly decreased in the autism samples relative to matched controls ($p=0.02$). Supporting H3K27 demethylation and increased *EN-2* gene expression, mean level of H3K4 trimethylation was found to be increased and the binding of GATA-1 enhancer element was decreased. The unexpected gene and protein over-expression in the presence of promoter DNA hypermethylation may be partially explained by over-riding histone methylation patterns in H3K27 and H3K4.

Conclusions: The epigenetic evaluation of *EN-2* in the autism cerebellum herein indicates a persistent up-regulation of this developmentally expressed homeobox gene that normally undergoes perinatal down-regulation to insure normal timing and onset of Purkinje cell differentiation.

Together, the results suggest that normal *EN-2* down-regulation that signals Purkinje cell maturation during late prenatal and early post-natal development may not have occurred in some individuals with autism and that the postnatal persistence of *EN-2* overexpression may contribute to cerebellar abnormalities in these individuals.

159.007 7 An Integrative Epigenome-Wide Autism Association Study. C. Ladd-Acosta^{*1}, A. R. Runarsson², J. Bonner³, B. K. Lee⁴, L. A. A. Croen⁵, L. A. Schieve⁶, D. E. Schendel⁷, A. P. Feinberg² and M. D. Fallin¹, (1)*Johns Hopkins School of Public Health*, (2)*Johns Hopkins University*, (3)*Michigan State University*, (4)*Drexel University School of Public Health*, (5)*Kaiser Permanente Division of Research*, (6)*National Center on Birth Defects and Developmental Disabilities*, (7)*National Center on Birth Defects and Developmental Disabilities, CDC*

Background: It is becoming clear that in order to understand the complex molecular architecture of autism it is important to examine and relate specific environmental exposures, genome-wide genetic, and epigenomic data. While the value of an integrated approach is now widely recognized, very few autism studies have compiled this information, especially from the same individuals. The Study to Explore Early Development (SEED) is one of the only case-control epidemiologic studies of autism with comprehensive phenotypic evaluation, broad prenatal environmental exposure information, genome-wide genotyping data, and whole blood available for epigenomic measurements, from the same individuals. Thus, we utilize samples from SEED to carry out the first large-scale effort to integrate genetic, environmental exposure, and epigenetic data and further our understanding of the molecular basis of autism.

Objectives: The overall purpose of this study is to identify sites of altered DNA methylation (DNAm) associated with autism and relate them to genome-wide genetic and prenatal environmental exposure data from the same individuals. In addition, we plan to evaluate DNAm as a potential biological mechanism for gene-environment interactions identified in our parallel SEED gene-environment-wide interaction study, using measurements from the same individuals.

Methods: Genotypes for 606 autism cases and 742 controls were measured using the Illumina 1M-Quad and Affymetrix Axiom arrays. Several quality control steps were implemented, at both the sample and SNP level, and SNP imputation was performed with IMPUTE2 using all individuals in the 1000 Genomes Project as a reference, resulting in genotyping data at over 13 million loci for 1,348 SEED children. We will focus on 5 specific *in utero* exposures (collected via maternal self-report using a structured interview) including

maternal use of tobacco, alcohol, β -2 adrenergic receptor agonist or antidepressant medications, and maternal infection. For 600 SEED children, we will measure DNAm using the Illumina Infinium 450K methylation platform. A data quality control pipeline, already developed, will be implemented to remove potential methylation measurement errors at both the sample and locus level. Analyses to identify sites of altered DNA methylation associated with autism, environmental exposures, and genotypes will be performed using a previously described analytic framework and generalized regression models.

Results: We are currently measuring DNA methylation for 600 SEED children (292 cases and 318 controls) with comprehensive phenotyping, genome-wide genotyping, and prenatal environmental exposure data already available. Analyses will be performed to: (1) identify genomic regions associated with altered methylation in autism; (2) find differentially methylated regions (DMRs) of the genome associated with specific *in utero* environmental exposures; (3) correlate autism and exposure associated DMRs with genotypes; and (4) assess DNAm as a potential biological mechanism for gene-environment interactions recently identified in our parallel SEED gene-environment interaction study, using data from the same individuals. Results from these analyses will be presented at the conference.

Conclusions: We present the first autism study to examine and relate genome-scale methylation, genotyping, and *in utero* environmental exposure data from the same individuals. Our integrated approach will likely provide a more comprehensive understanding of the molecular underpinnings of autism.

159.008 8 Identification of Gene-Environment Interactions Associated with Autism. M. D. Fallin^{*1}, B. K. Lee², J. Bonner³, B. Sheppard¹, N. B. Gidaya⁴, L. A. Weiss⁵, J. Quinn⁵, G. C. Windham⁶, A. M. Reynolds⁷, L. A. A. Croen⁸, D. E. Schendel⁹, C. J. Newschaffer² and C. Ladd-Acosta¹, (1)*Johns Hopkins School of Public Health*, (2)*Drexel University School of Public Health*, (3)*Michigan State University*, (4)*Drexel University*, (5)*University of California San Francisco*, (6)*California Dept of Public Health*, (7)*University of Colorado Denver*, (8)*Kaiser Permanente Division of Research*, (9)*National Center on Birth Defects and Developmental Disabilities, CDC*

Background: There is increasing interest in understanding genetic and environmental risk factors and their interplay in autism. However genome-wide gene-environment interaction studies have been hindered in the past mainly due to the lack of specific exposure and genome-wide genotyping data from the same individuals. Here we utilize a unique sample source to examine gene-environment interactions in autism: The Study to Explore Early Development (SEED). SEED is one of the only multi-site case-control autism studies with comprehensive phenotyping and genome-wide genetic and prenatal environmental exposure data for thousands of children.

Objectives: The main purpose of this study is to identify genetic and environmental factors that influence risk for autism. More specifically, we sought to: (1) identify SNPs whose effects on autism risk vary across levels of selected prenatal environmental exposures; and (2) assess copy number variation (CNV) in SEED children to identify CNVs associated with autism.

Methods: For our GxE analysis, we examined prenatal exposures across four domains including maternal use of tobacco, alcohol, and medication (B2ARs and SSRIs) as well as maternal infection. Prenatal environmental exposure information was derived from maternal self-reported data using a structured interview. Genotypes for 1,348 SEED children (606 cases and 742 controls) were measured using HumanOmni1 and Affymetrix Axiom arrays. After applying data quality control measures, and performing imputation to obtain > 6 million genotypes per person, initial analysis was performed using a new joint likelihood ratio test for marginal genetic main effects and gene-environment interaction. For our CNV analysis, we utilized PennCNV to call copy number variants from the SEED genotyping array data and to perform overall CNV burden analyses. We have also performed association tests to identify autism-specific CNVs.

Results: Our preliminary GxE analysis, using data from 873 SEED children, revealed a genome-wide significant ($P < 5 \times 10^{-7}$) interaction between genotype and smoking for several neighboring SNPs on chromosome 2. In a similar subset of SEED samples, we found a significant ($P = 0.006$) increase in the overall global burden of large rare

CNVs in cases relative to controls and identified autism-associated amplifications and deletions in genes previously implicated in autism. We are currently in the process of completing our final GxE and CNV analyses for the complete set of 1,348 SEED samples and will present our findings at the conference.

Conclusions: We have identified copy number variants and interactions between genomic regions and specific *in utero* environmental exposures that are associated autism. This suggests coupling genetic and environmental exposure information to determine autism risk is more fruitful than looking for genetic marginal effects alone. SEED has proven to be a particularly useful resource for these types integrative of studies.

159.009 9 Genome-Wide DNA Methylation Profiles in Post-Mortem Brains From Subjects with Autism. K. Iwata*¹, H. Matsuzaki², K. Nakamura¹ and N. Mori¹, (1)Hamamatsu University School of Medicine, (2)Research Center for Child Mental Development, Hamamatsu University School of Medicine

Background: Autism is a developmental disorder characterized by severe and sustained impairment in social interaction and communication, and restricted or stereotyped patterns of behavior and interest. This disorder is more prevalent in males than in females. Although twin studies have provided evidence for a strong genetic component for the condition and many candidate genes have been reported, the underlying genetic role and its mechanism have yet to be determined. Recently, it has been reported that genetic heritability is lower than that previously estimated, and environmental factors also have a greater influence on the development of autism. Epigenetic processes such as DNA methylation and histone modification are considered to be an interface of genetic and environmental factors. Additionally, two well-characterized epigenetic processes, parental imprinting and X chromosome inactivation, are known to be involved in several conditions that mimic autism spectrum disorders, such as Angelman, Prader-Willi, 15q duplication, Rett and Fragile-X syndromes. This clinical evidence suggests that epigenetic processes may play an important role in the pathophysiology of autism. Thus, we investigated genome-wide DNA methylation profiles in post-mortem brain tissue from individuals with autism.

Objectives: Dorsal raphe from 6 male subjects with autism and 7 age- and sex-matched healthy control subjects.

Methods: We measured methylation levels of CpG sites in these samples using Infinium HumanMethylation450 BeadsChip.

Results: We found significantly elevated levels of methylation in 44 CpG-sites in 40 gene regions and significantly decreased levels of methylation in 37 CpG-sites in 34 gene regions in subjects with autism compared to controls. Some of these genes, such as *DAB1* and *GRIA1*, have been implicated in autism and other developmental disorders (Fatemi *et al.*, 2005; Ayalew *et al.*, 2012). We subsequently examined to see whether modifications would be present especially on sex chromosome and altered levels of methylation were found in CpG-sites in chromosome X, but not in chromosome Y.

Conclusions: In this postmortem study, we found significant differences in DNA methylation profiles between the brains of autism and control subjects. The abnormal DNA methylations, especially gene regions implicated in autism and other developmental disorders, may underlie the pathophysiology of autism. Moreover, in sex chromosomes, abnormal DNA methylations only in X chromosome may account for the unequal sex ratio in autism.

159.010 10 Epigenetic and Related Transcriptional Alterations

Affecting Chromatin Remodelling and Synaptic Genes in Autism Spectrum Disorders. A. Homs^{*1}, I. Cusco², B. Rodríguez-Santiago³, C. M. Villanueva⁴ and L. A. Pérez-Jurado², (1)*The Centre for Biomedical Network Research on Rare Diseases (CIBERER)*, (2)*Instituto de Investigación Sanitaria IMIM-Hospital del Mar*, (3)*Quantitative Genomic Medicine Laboratories, S.L. (qGenomics)*, (4)*Biomedical Research Centre Network for Epidemiology and Public Health (CIBERESP)*

Background: Autism Spectrum Disorders (ASD) are highly heritable and genetically complex conditions with likely environmental contribution. Although multiple candidate genes have been identified, they only account for the aetiology of 15-20% of cases so far. Additional evidence in support of an epigenetic contribution to ASD include the epigenetic deregulation in single-gene disorders associated with autism (i.e. Fragile X and Rett syndromes) and alterations in several

chromosomal regions subjected to imprinting (chr7q, 15q). High throughput methylome studies have recently revealed a possible contribution of epigenetics to the molecular basis of ASD.

Objectives: To explore the role of epigenetics in ASD by defining genome-wide methylation alterations along with their correlation with genetic and/or expression abnormalities in a cohort of idiopathic ASD.

Methods: We quantified global 5-methylcytosine (5mC) content by HPLC-MS and studied genomic methylation patterns by using the Illumina Infinium HumanMethylation 450K array in peripheral blood DNA from ASD patients (n=34, males, 2-15 year old, idiopathic aetiology) and controls (n=101). We also studied transcriptome expression in whole blood by RNAseq (n=19), and exclude possible genetic alterations (aCGH and exome sequencing). Functional annotation by enriched gene ontology-based analysis was performed with CPDB.

Results: We found that the genomic content of 5mC was significantly reduced in ASD with respect to age-matched controls (2.62+/-0.4 vs 4.06+/-0.16). The methylation high-throughput profile did not show remarkable global epigenetic alterations. After extensive filtering (discarding genetic alterations) and statistical analyses, we observed **427 genes containing differentially methylated CpGs (DMCpG) compared to controls (p-value<0.01). Most DMCpG showed relative hypomethylation in ASD (90%),** in agreement with 5mC quantification. Among these 427 loci, **41 (10%) had been previously associated with ASD** by genetic or genomic rearrangements, further reinforcing their putative role in the disease. Functional annotation revealed enrichment of **genes involved in the glutamate neurotransmitter release cycle, mTOR signalling, synaptic plasticity, neuron projection, synapse organization and axon guidance.**

Analysis of the putative transcriptional effects in *cis*, 50Kb up or downstream the target CpG, revealed **expression changes in 10% of surrounding genes**, including additional candidates coding for chromatin remodelling complexes (*HR* and *SETD1A*), synaptic

transmission (*STX1B*), or linked to ASD by genetic studies (*AGRP*).

The analysis of the most relevant CpG sites by scalable techniques in a larger cohort of patients and controls is in process.

Conclusions: Our data provide support for the hypotheses that epigenetic abnormalities may be pathogenically related with ASD in a significant proportion of cases, either as primary or secondary (genetic) events. Genes acting at the synapse and chromatin remodelling factors are differentially methylated in autism and show abnormal expression.

Clinical Phenotype Program

160 Clinical Phenotype

Moderator: L. Gallagher Trinity College Dublin

This session gives an overview of multiple factors impacting on presentations in autism spectrum disorders including gender, lifespan, trajectories and cultural factors. Research on clinical features associated with ASD but not typically considered central to the diagnosis is also presented.

160.011 11 Adaptive Behavior and IQ: A Developmental Trajectory Analysis of Individuals Served by the Teacch Autism Program From 1965-2000. A. T. Meyer*¹, P. S. Powell², L. G. Klinger³ and M. R. Klinger², (1)*University of North Carolina-Chapel Hill*, (2)*University of North Carolina - Chapel Hill*, (3)*University of North Carolina*

Background:

As the number of children diagnosed with Autism Spectrum Disorder (ASD) rises, there will be an increasingly large adult population. Although families often ask about long-term outcome, few studies have followed individuals diagnosed in childhood into adulthood. Previous studies have used a cross sectional approach or only followed individuals into early adulthood. For example, using a cross sectional design, Mayes and Calhoun (2003) found that IQ increased until around 8 years and then plateaued. Using a longitudinal design, Smith et al (2012) found that adaptive behavior improved during adolescence but then plateaued in early adulthood. More longitudinal research is needed to examine whether these skills truly plateau during development.

Objectives:

The database for the TEACCH Autism Program was created in 1965 and includes a large sample (N=400) of individuals with ASD who were evaluated multiple times across development. The purpose of this study is to examine the longitudinal course of adaptive behavior and IQ for individuals diagnosed with ASD between 1965 and 2000.

Methods:

Participants were assessed longitudinally at 3 or more times throughout childhood extending into adulthood (assessments conducted on individuals ranging in age from 1 – 36 years). All participants had scores from the Children Autism Rating Scale (CARS), age appropriate IQ, and Vineland Adaptive Behavior Scales. IQ scores averaged 56.31 (range 20-122). Hierarchical linear mixed model analyses were conducted on mental ages derived from IQ (n=156) and adaptive behavior (n=168) measures. Data entry is ongoing with additional participants.

Results:

Hierarchical linear mixed model analyses used chronological age to predict mental age derived from IQ and adaptive behavior measures. Both the linear and quadratic components of age were examined. For intellectual mental age, the linear component of chronological age significantly predicted mental age. The slope of the chronological age effect was approximately .40 ($p < .001$) indicating that for every year of chronological age, participants increased approximately 5 months in mental age. For adaptive behavior age equivalent, both the linear and quadratic effects of chronological age were significant ($p < .001$). Across young ages (2 to 9 years), adaptive behavior age increased at a similar rate to intellectual mental age (approximately 5 months improvement for every year of chronological age). From age 9 to 18 years the slope becomes shallow with approximately 3 months gain in adaptive functioning for every year of age. After age 18 years the slope becomes flat (no gain in functioning with age) to a slightly negative slope that may indicate a loss in adaptive functioning age.

Conclusions:

Findings suggest that both intellectual ability and adaptive behavior increased during early childhood commensurate with predictions based on IQ. However, during adolescence adaptive behavior appears to slow and then plateau or declines at entry into adulthood. These results have important implications for long-term outcome (employment and independent living skills) that rely on adaptive behavior skills.

160.012 12 New ADI-R Algorithms for Children and Young People with ASD: Implications for DSM-5. A. Le Couteur*, P. James, D. Hammal and H. McConachie, *Newcastle University*

Background:

The Autism Diagnostic Interview- Revised (ADI-R) is a standardised semi-structured interview that provides a framework for the developmental history needed when considering diagnosis of an Autism Spectrum Disorder (Lord et al, 1994; Rutter et al, 2003). The ADI-R has also been widely used as a measure of the autism phenotype in research studies and as a criterion in validity studies of other measures. The published version provides a diagnostic algorithm for ICD-10 childhood autism only, with no algorithm for the broader diagnosis of ASD. In 2013 DSM-5 will be published with new diagnostic criteria for ASD.

Objectives:

This paper presents the findings from an exploratory factor analysis, proposes algorithms for ASD and considers the impact of the new DSM 5 criteria on current clinical and research practice.

Methods:

A dataset was collated from nine clinical academic and research centres (8 UK; one US). The subjects were aged from 18 months to 19 years at time of assessment. The combined dataset includes children referred for diagnostic evaluation for ASD, or recruited to genetic or intervention studies, children attending speech and language specialist education, children with conduct disorder and a school based general population study. Exploratory Factor Analysis was conducted using MPLUS, to investigate the underlying factor structure of the ADI-R and the results informed

the selection of items to create an algorithm for the diagnosis of ASD. Further analyses were undertaken to investigate the performance of the new algorithms with respect to the child's original research descriptor, age, gender, language and cognitive ability.

Results:

Complete data on 873 participants were used to investigate the underlying factor structure of the ADI-R. Additional samples of 270 individuals with autism and 92 typically developing children were available for external validation. The factors were rotated with a PROMAX transformation in order to maximise the contrast in factor loadings. Models with 2 factor solutions with Root Mean Square Error (RMSEA) of 0.052 for non-verbal and 0.050 for verbal cases were the best fit. This 2-factor solution was used to design the ASD algorithms. Threshold cut-off scores were identified using Receiver Operating Characteristic (ROC) curves to maximise sensitivity and specificity. Algorithm cut-offs achieved good discrimination for children with a research diagnosis of ASD.

Conclusions:

A 2- factor structure, with domains labelled "Social Communication" and "Stereotyped Speech, Rigidity and Repetitive Behaviour", was identified using ADI-R items and new algorithms were successfully developed with high sensitivity and specificity for autism and ASD. The implications of these findings will be discussed in relation to the DSM5 criteria for ASD and the wider impact on diagnosis for children and young people from preschool to older adolescence.

This work was funded by the Health Foundation with additional support from Northumberland Tyne and Wear NHS Foundation Trust flexibility and sustainability funding .

160.014 14 Sensory Features in Autism: Physiological and Behavioral Characterization. R. Schaaf* and T. Benevides, *Thomas Jefferson University*

Background: Sensory hypo and hyper-responsivity, and unusual sensory interests are extremely prevalent (80-90%) in individuals with Autistic Spectrum Disorder (ASD) and present some of the most challenging obstacles by limiting

adaptive behaviors and participation in life activities. They are now proposed to be included as a core feature for diagnosis of Autism Spectrum Disorders (ASD) under the Restricted and Stereotypic Behavior criteria in the DSM 5 (APA, 2012). As such, objective markers of these features have new and important relevance for diagnosis and treatment of ASD.

Objectives: This paper reports on the results of an NIH-funded study that evaluated physiological and behavioral responses to sensation in 59 phenotypically characterized subjects with ASD, 6-9 years of age in comparison to 30 age and IQ matched controls. The aims of this study were to 1) evaluate sympathetic and parasympathetic activity at baseline and during sensory challenges in comparison to typically developing controls to determine if physiological activity during sensory stimuli is a unique feature of ASD; and 2) evaluate whether physiological reactions to sensation are related to (or predict) behavioral responses to sensation and/or adaptive behavior.

Methods: Fifty-nine children diagnosed with ASD and confirmed with the ADI-R were tested during the Sensory Challenge Protocol, a unique laboratory procedure designed to assess autonomic nervous system activity in response to sensory challenges in the auditory, tactile, olfactory, visual and vestibular systems. Parasympathetic activity was measured via heart rate variability, and sympathetic activity was measured via pre-ejection period as described by Berntson, Cacioppo and colleagues (1995). Behavioral responses to sensation were measured by the Short Sensory Profile and the Sensory Processing Measure; and The Vineland Adaptive Behavior Scales-II were used to assess adaptive behaviors. Mixed effects linear regression was used to jointly model RSA and PEP scores at each domain by group. Within the mixed effects model, we performed several multivariate hypothesis tests. First, we tested for any difference between groups at any domain with respect to mean RSA/PEP. Second, we tested for any difference between groups with respect to change in RSA/PEP from the previous domain. If the multivariate tests were significant, we proceeded to perform group comparisons at each domain. In addition, multiple linear regression analyses estimated the association between behavioral scores (the dependent variables) and

physiological measures controlling for severity of ASD, gender, and mental age and IQ.

Results: Subjects with ASD show significantly less parasympathetic reactivity during the sensory challenges and a trend for elevated sympathetic activity. Data analysis of physiological-behavioral relationships is currently being completed and will also be reported. We expect that decreased parasympathetic activity and increased sympathetic activity will be related to greater sensory dysfunction and poorer adaptive behavior.

Conclusions: Objective characterization of sensory features in ASD may provide important clues regarding the mechanisms of these sensory features and provide insight into intervention targets for these behaviors.

160.015 15 Multiplex Versus Simplex Autism: Different Phenotypic Severity. C. Amiet^{*1}, J. Carayol², B. Génin², V. Guinchat¹ and D. Cohen¹, (1)*Groupe Hospitalier Pitié-Salpêtrière, APHP*, (2)*IntegraGen SA*

Background:

Autism spectrum disorders (ASD) are among the most common forms of severe developmental disability with a prevalence of 1 in 150 children. The inheritance pattern of ASD in most families is complex and not compatible with simple Mendelian inheritance. It may also vary according to gender and comorbidities (e.g. seizures, IQ). Recent studies have suggested disparate clinical and genetic settings depending on a simplex autism (only one affected family member) or a multiplex autism (two or more affected family members) definition.

Objectives:

This study aimed to explore whether the phenotype varies depending on the presence or absence of affected siblings.

Methods:

A total of 2,396 children (2,080 males, 316 females) from the Simons Simplex Collection (SSC) and 2,247 children (1,808 males, 439 females) from the Autism Genetic Resource Exchange (AGRE) multiplex database were

examined. The SSC includes families with only one child diagnosed with ASD (simplex autism), and probands with mental age below 18 months were excluded. The AGRE includes families with two or more members diagnosed with ASD, Pervasive Developmental Disorder-Not Otherwise Specified or Asperger's syndrome. The following variables were extracted for comparisons: the Autism Diagnostic-Interview-Revised (ADI-R) sub scores, the Vineland Adaptive Behaviors Scales (VABS), and the presence of epilepsy.

Results:

Mean VABS composite standard scores were found to be significantly lower in multiplex ASD than simplex ASD (OR=0.94; 95% confidence interval (CI):0.93-0.94). Children with multiplex ASD were also found to have more first word delay (OR=1.7, 95%CI:1.5-2.0) and a lower overall level of language (OR=2.2, 95%CI:1.9-2.4). While adjusting for adaptive level, the difference remains significant. Considering ADI-R scores, repetitive and stereotyped behavior scores were found to be significantly lower in multiplex ASD than simplex ASD (OR=0.88, 95%CI:0.85-0.9). Non-verbal communication scores were found to be significantly higher in multiplex ASD than simplex ASD (OR=1.12, 95%CI:1.09-1.15). Finally, epilepsy was more frequent in multiplex ASD than simplex ASD.

Conclusions:

Multiplex and simplex autism may be defined by a difference in phenotype severity with children with multiplex autism found to show more adaptive and language impairment, less repetitive and stereotyped behaviors, and more epilepsy.

160.016 16 Using the Communication Checklist –Adult (CC-A) to Identify Pragmatic Impairment in High-Functioning Young Adults with ASD (HFA): Preliminary Results. W. Mitchell* and J. Volden, *University of Alberta*

Background:

Communication impairment is one of the core features of autism spectrum disorder (ASD), yet we know very little about the communicative profile of high-functioning (i.e. those without intellectual disability; HFA) adults with ASD. In **children** with HFA, pragmatic dysfunction,

defined as difficulty in the appropriate and social use of language, persists even when scores on traditional tests of language competence are within normal limits (Landa, 2000, Volden & Phillips, 2010). Functionally, pragmatic impairment negatively influences the establishment of friendships (Landa, 2000). One difficulty is finding measures of language competence and pragmatic impairment that are appropriate for adults. The pragmatic subtests (Pragmatic Judgment, Non-Literal Language) from the Comprehensive Assessment of Spoken Language (CASL; Carrow-Wolffolk, 1999) may be useful (Reichow, et al., 2008), but to date, the CASL has not been used with the adult HFA population. In addition, Whitehouse & Bishop (2009) have recently developed a checklist, completed by an informant that knows the affected adult well, called the Communication Checklist – Adult (CC-A) and found that it was able to identify adults with communication disorders. No studies have yet been conducted using these measures on young adults with ASD.

Objectives:

This pilot study examines communicative performance in adults with HFA using a battery of language and communication measures. Performance on the CASL and the CC-A is expected to reveal deficits in pragmatic skill while participants may or may not demonstrate difficulties in language syntax or vocabulary.

Methods:

Five adults (18- 30 years) with confirmed diagnoses of ASD based on the Autism Diagnostic Observation Schedule (ADOS; Lord et al.,2003) and performance IQs above 80 based on the Weschler Abbreviated Scale of Intelligence;(WASI; Weschler, 1999) were given a battery of language tests. Syntax and vocabulary abilities were determined using subtests from the Test of Adolescent and Adult Language - 4 (TOAL-4; Hammill, et al., 2007). Pragmatic abilities were measured using pragmatic subtests from the CASL (Carrow-Wolffolk; 1999) and the CC-A.

Results:

As expected, mean standard scores on syntactic (10.2, 8.4) and semantic (11.6, 8.4, 8.0) subtests from the TOAL were all within the average range (10 + / - 3). Surprisingly, mean performance on pragmatic subtests from the CASL (96, 86) were also within the average range (100 + / - 15). Mean scaled scores from the CC-A, however, indicated abnormality (scaled scores < 6) on the Pragmatic Skills (mean scaled score = 5.2) and Social Engagement (mean scaled score = 3.2) subscales.

Conclusions:

For this pilot sample of adults with HFA, neither the conventional standardized language measures nor the CASL detected communicative impairment. This contrasts sharply with results from the CC-A. Whitehouse & Bishop (2009) note that impaired scores on 2 or more subscales are indicative of communication difficulties that will influence everyday life. If these results are confirmed in larger studies, clinicians should include the CC-A in the evaluation of communicative profiles of adults with ASD in order to capture the kinds of communicative difficulties that may influence a person's ability to participate in the community.

160.017 17 Social Communication and Autistic Triad Trait Patterns in Preschoolers with Severe Visual Impairment. N. J. Dale*¹, R. MacKechnie² and A. Salt¹, (1)Great Ormond Street Hospital NHS Foundation Trust, (2)UCL Institute of Child Health

Background:

Severe visual impairment (VI) is associated with significant difficulties in social communication; 11-40% of children with VI are diagnosed with autism spectrum disorder (ASD). Relatively little is understood of the nature and aetiology of social communication and ASD in VI. Of debate is whether children with VI and ASD have a similar phenotype to Sighted ASD children or whether there are qualitative differences. There have been few systematic studies of the social communicative phenotype of young children with VI due to methodological challenges and population rarity.

Objectives:

Using a newly developed and validated Visual Impairment Social Communication schedule (VISS) (Absoud et al 2010), this study aims to investigate the social communicative phenotype of preschoolers with severe VI. Patterns within the triad traits are considered in the context of 'At Risk' or 'Not At Risk' for ASD diagnosis, vision level (profound; severe VI) and developmental quotient (DQ).

Methods:

A consecutive clinic sample of 35 preschoolers with VI (mean age 39.4 months, range 1.5 to 5 years) attending a specialist paediatric developmental vision clinic was included. A trained Research Assistant used the observational VISS to code social interaction (SI), communication and language (C) and play and behaviour (B) during the play based assessment with the clinician. The coded data was entered into a database and the sample was divided into 'At Risk' and 'Not at Risk' of ASD subgroups, according to whether they scored above or below the clinical threshold on total VISS score (Absoud et al). Statistical analysis was undertaken between and within the two subgroups.

Results:

43% of the sample was found to be 'At Risk' and 57% 'Not At Risk' for ASD, with a significant difference in mean score, indicative of a bimodal distribution. A mixed between-within subjects analysis of variance revealed that children 'At Risk' performed consistently worse across all triadic domains, in comparison to children 'Not at Risk', $F(1, 33) = 107.05, p < .0005$, partial eta squared = .76. A main effect for triadic area was also revealed (Wilks Lambda = .62 $F(2, 32) = 9.78, p < .0005$, partial eta squared = .38), with both groups showing more impairments in C relative to SI and B domains. The triad domains were significantly positively correlated within the 'At Risk' group, whereas there were no significant associations in the 'Not at Risk' group. DQ was not associated with VISS scores in either group.

Conclusions:

43% of the sample was found to be 'At Risk' for ASD, in line with previous studies. As in classical

Kanner's autism, the scores were extremely low across all three triad domains, suggesting that VI-ASD phenotype was similar to the phenotype of Sighted-ASD preschoolers. However, both the 'At Risk' and 'Not At Risk' subgroups showed a greater impairment in social communication relative to social interaction and behaviour domains. This finding argues for possible 'fractionation' of the triad in the more successfully developing preschoolers and raises important theoretical questions about the vulnerability and aetiology of social communication and ASD in VI preschoolers.

160.018 18 A Cross-Cultural Comparison of Autistic Traits: UK, India, Malaysia. M. Freeth*¹, E. Sheppard², R. Ramachandran³ and E. Milne⁴, (1)*University of Sheffield*, (2)*University of Nottingham Malaysia Campus*, (3)*University of Calicut*, (4)*The University of Sheffield*

Background:

Autism is widely recognised throughout the world but the diagnostic criteria and theories of autism are based on research predominantly conducted in Western cultures. However it is important to consider that what is typical may differ between cultures. Indeed, significant differences in behaviour and cognition have been observed between individualist and collectivist cultures. Hence the point at which normal variability differentiates from an actual disorder, such as an ASD, is likely to be influenced by cultural values and norms. Cross-cultural comparative studies are required to fully understand the impact of culture on behaviour and therefore whether behaviours that are included in autism diagnosis in Western cultures are also considered atypical in non-Western cultures.

Objectives:

To identify possible cultural differences in the expression of autistic traits between one Western, individualist culture (UK) and two Eastern, collectivist cultures (India and Malaysia).

Methods:

The Autism-spectrum Quotient (AQ) was completed by neurotypical undergraduate and postgraduate university students across three

countries (UK n=723; India n=271; Malaysia n=245).

Results:

Behaviours associated with autism were reported to a greater extent in the Eastern cultures than the Western culture (UK mean score = 17.2; India mean score = 21.2; Malaysia mean score = 21.7). Males reported more autistic traits than females, and science students reported more autistic traits than non-science students in each culture. Indian students reported more autistic traits than both other groups on the Imagination sub-scale, Malaysian students reported more autistic traits than both other groups on the Attention Switching sub-scale. Similarities in empirically derived factor structures emerged between groups, with each group displaying a clear "social enjoyment" factor. Social communication and attention to detail also emerged strongly in each of the cultures, though these factors appeared to be more closely linked in the Eastern samples than in the UK sample. Imagination emerged as a factor in the UK and Malaysian samples but not in the Indian sample.

Conclusions:

Behaviours associated with the broader autism phenotype are more prevalent in collectivist cultures than individualist cultures. Differences were also observed between cultures in how behaviours associated with different aspects of autism grouped together. It is therefore clear that behaviours associated with autism are strongly influenced by culture. We propose that differences in social structure and cultural interpretation strongly contribute to observed differences. As each of the samples were drawn from academically successful individuals (students) it is also clear that possessing slightly more autistic traits is not detrimental to academic success in collectivist cultures and may even be valued.

160.019 19 Peers' Evaluation of Stories Told by Optimal Outcome Children with a History of Autism Spectrum Disorders. J. Suh*¹, I. M. Eigsti¹, L. Naigles¹, M. Barton¹, A. Orinstein¹, K. E. Tyson¹, E. Troyb¹, M. Rosenthal², M. Helt¹, R. T. Schultz³, M. C. Stevens⁴, E. A. Kelley⁵ and D. A. Fein¹, (1)*University of Connecticut*, (2)*Child Mind Institute*, (3)*Children's Hospital of Philadelphia*, (4)*Institute of Living, Hartford Hospital / Yale University*, (5)*Queen's University*

Background: A study is following children who have a history of autism spectrum disorder (ASD), but who no longer meet diagnostic criteria for such a disorder. These children 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 ASDs, achieve "optimal outcomes" (OO; Sutera et al., 2007; Helt et al., 2008; Kelley, Naigles, & Fein, 2010); however, pragmatic language skills may continue to show subtle impairments.

Objectives: Narratives are a highly sensitive tool for examining language skills. In order to assess potentially very subtle variability in pragmatic language ability, we asked high school students to read transcriptions of the *Tuesday* story and to evaluate them qualitatively for "story goodness."

Methods: Forty-five participants with high-functioning autism (HFA; n=15), typical development (TD; n=15) or OO (n=15) completed the *Tuesday* story narration. Participants were matched on age (mean=12.8, range 9-15) and verbal IQ. Narratives were transcribed by coders naïve to diagnosis. Transcriptions were read by five adolescents (ages 15-17), naïve to diagnosis, who rated the narratives on a five-point scale (1= poor, 5= excellent) according to: overall quality of story, story flow, comprehension, sophistication of language, correct use of grammar, story imagery, energy level, engagement level of the story, clarity of story content, and presence of oddity in wordings and themes.

Results: ANOVA tested for group differences in peer story ratings. The OO and HFA groups' ratings were significantly lower than TD group for: overall narrative quality [M(SD)= 3.1 (0.5), 3.0 (0.5), and 3.5(0.5) for OO, HFA, and TD, respectively; $p = .03$]; story flow [2.9 (0.7), 2.7 (0.6), and 3.4 (0.4); $p < .01$]; and comprehension [3.1 (0.5), 3.1 (0.5), and 3.7 (0.4); $p < .01$]. The HFA group received significantly lower scores than both OO and TD groups for sophistication of language [3.4 (0.5), 3.0 (0.5), and 3.4 (0.3); $p = .04$]. The HFA group received significantly lower scores than the TD group on grammatical structure; the OO group did not differ from either group [3.1 (0.4), 2.9 (0.4), and 3.3 (0.3); $p = .02$]. There were no group differences in any other narrative characteristics.

Conclusions: *Tuesday* narrations were evaluated in a previous study (Suh et al., 2012, INS presentation) for subtle aspects of pragmatic language such as clarity of pronoun use; the OO and TD groups did not differ on these measures. In this analysis, however, the OO group's narrations were evaluated by peers as having lower overall quality, overall flow, and being harder to comprehend relative to TD counterparts. Further data are being collected from additional raters to insure the reliability of rating scales. Despite having language and social skills in the average range, pragmatic language skills in OO may retain subtle deficits that are perceptible to untrained, lay interlocutors. This is meaningful, as peer interpretation of communications is crucial for social inclusion. We discuss implications of why these aspects of pragmatic language are so resistant to improvement.

160.020 20 Early Diagnostic Severity Is Predictive of Not Maintaining ASD Diagnosis. D. N. Abrams*, D. L. Robins and L. B. Adamson, *Georgia State University*

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. Studies have sought to identify features at initial diagnostic assessment that distinguish those who maintain a diagnosis from those who do not; however, findings have been varied. Some indicate that early communication abilities tend to predict positive outcomes better than symptom severity.

Objectives: To identify abilities and symptoms at 2-year-old evaluation that predict which children no longer meet ASD criteria by age 4.

Methods: 73 children were evaluated at age 2 (T1, $M=26.24$ months, $SD=4.42$) and re-evaluated near age 4 (T2, $M=47.79$ months, $SD=6.22$) after screening positive on the Modified Checklist for Autism in Toddlers (M-CHAT; Robins et al., 1999) or being flagged for possible ASD. Evaluations included ADOS, ADI-R, CARS, Vineland Adaptive Behavior Scales-II (VABS), and Mullen Scales of Early Learning (MSEL). Children received a diagnosis of ASD, nonASD developmental delay, or no diagnosis. At T1, 49 received an ASD diagnosis and 24 did not. At T2, 12 (24%) of the children diagnosed with ASD at T1 no longer met criteria for an ASD (ASD-NON), and 37 maintained an ASD diagnosis (ASD-ASD);

20 maintained non-ASD status (NON-NON). Four children who did not receive an ASD diagnosis at T1 were diagnosed at T2; they were excluded here due to small sample size.

Results: A repeated-measures ANOVA revealed that groups differed in ADOS comparison scores, with a significant group x time interaction, $F(1,2)=28.29$, $p<.001$. In children who received an ASD diagnosis at T1, logistic regression revealed that those with lower ADOS comparison scores at T1 were more likely to no longer meet criteria at T2, $OR=.641$, $p=.048$. ASD-ASD and ASD-NON groups differed at T1 on DSM-IV total symptom count, $F(1,47)=6.832$, $p=.01$, social impairment symptoms, $F(1,47)=6.62$, $p=.01$, and RRB symptoms, $F(1,46)=4.54$, $p=.04$. Lower symptom counts predicted no longer meeting criteria at T2, $OR_{total}=.48$, $p=.02$; $OR_{social}=.37$, $p=.02$; $OR_{RRB}=.36$, $p=.047$. Surprisingly, VABS daily living skills were predictive of not maintaining a diagnosis; as scores increased, odds of no longer meeting criteria decreased, $OR=9.31$, $p=.045$. MSEL developmental quotient, VABS adaptive behavior composite, and DSM-IV communication symptom count were not predictive of diagnostic instability ($ps>.05$).

Conclusions: In contrast to some of the existing literature, metrics of diagnostic severity of ASD symptoms at 2-year-old evaluation, including the ADOS comparison score and DSM-IV symptom count, were predictive of not maintaining an ASD diagnosis. Language and cognitive abilities, however, were comparable between groups who did and did not maintain ASD diagnosis. These findings imply that the lack of diagnostic stability in the ASD-NON group is due to true differences in ASD symptom severity, and is not simply explained by differences in cognitive and language skills at initial evaluation. Future research should examine whether other factors, such as intervention type and intensity, contribute to predictions of diagnostic stability.

160.021 21 Sex Differences in the Expression of Autism Spectrum Disorders in Children. J. Shenouda^{*1}, S. Neves², H. Patel², P. Khandge³, R. Baltus⁴ and W. W. Zahorodny⁵, (1)UMDNJ-New Jersey Medical School, (2)New Jersey Autism Study, (3)New Jersey Medical School- University of Medicine & Dentistry of New Jersey, (4)New Jersey Medical School - University of Medicine & Dentistry of New Jersey, (5)New Jersey Medical School

Background: Epidemiologic studies consistently show that males are disproportionately affected by Autism Spectrum Disorder (ASD) and that girls with ASD are more likely than boys to be cognitively impaired. Sex differences in the clinical expression of ASD have not been elucidated, however.

Objectives: The purpose of this study was to examine sex-based differences in the clinical expression of ASD in a large, population-based, sample.

Methods: Data from three successive cycles (2000, 2002, 2006) of ASD surveillance in New Jersey, according to the Centers for Disease Control and Prevention (CDC) multiple source ascertainment method were analyzed to understand the expression of core ASD (social, communication and behavioral) dysfunctions (parsed according to DSM-IV-stipulated criteria) in boys and girls, and 2) to assess the effect of cognitive functioning, as indicated by intelligence quotient (IQ) scores, on the expression of ASD. Group differences were compared by Chi-square tests.

Results: 1,012 eight-year old children with ASD were identified and their data was analyzed. The sample was predominately male (males = 805, 79.5%; females = 207, 20.5%). Overall, there was no significant difference by race/ethnicity or SES between males and females. However, several sex-based differences in expression of core ASD characteristics were identified. In comparison to boys, girls were more likely to lack social or emotional reciprocity (72% vs. 62%, $p<.001$) and to lack spontaneous seeking to share enjoyment, interests and achievement (38% vs. 28%, $p<.01$). Girls showed more stereotypic language (73% compared to 60%, $p<.001$) and had a higher frequency of impaired imaginative/symbolic play (48% vs. 33%, $p<.001$). Girls were more likely to exhibit inflexible adherence to specific, nonfunctional routines or rituals (66% vs. 54%, $p<.01$), to have stereotyped and repetitive motor mannerisms (62% vs. 47%, $p<.001$) and, also, to have persistent preoccupation with parts of objects (34% vs. 20%, $p<.001$). Furthermore, when we analyzed the population according to whether the ASD cases had cognitive impairment (IQ below 70) or not (IQ above 70), many of the sex-based

differences in the expression of core ASD indicators were evident in the children with IQ above 70, but not in the children with IQ below 70.

Conclusions: Consistent with other epidemiologic studies, males with ASD outnumbered females by a ratio of 4.1:1. While boys and girls with ASD were equally likely to show deficits in non-verbal social behavior, peer relations, expressive and receptive language operations and to have equivalent levels of restricted interest, contrary to expectation, girls in our population had documented indication of all other core ASD indicators more frequently than boys. Understanding sex-based differences in the expression of ASD is important for the specification of autism phenotypes and for development of effective interventions. Additional research is needed to further investigate sex-based differences in the expression of ASD and to assess the influence of cognitive level on the expression of ASD.

160.022 22 Association of Early Generalized Overgrowth to Clinical Outcome in ASD. D. J. Campbell*¹, J. Chang² and K. Chawarska¹, (1)*Yale University School of Medicine*, (2)*Yale University*

Background: Accelerated rate of head circumference (HC) growth in infancy is a well-replicated but poorly understood phenomenon in autism spectrum disorders (ASD) (Courchesne et al, 2003; Fukumoto et al, 2008). A recent comprehensive study has shown that accelerated HC growth in boys with autism was accompanied by rapid overgrowth with regard to height and weight, representing a generalized overgrowth (Chawarska et al, 2011).

Objectives: In this study we replicate and extend our work on generalized overgrowth by examining the phenomenon of overgrowth in a larger sample of both boys and girls with ASD, as well as by examining the predictive associations between clinical features at the age of three and body size at birth as well as the rate of growth from birth to 24 months.

Methods: HC, height, and weight measurements were collected retrospectively from 347 children with autism (AUT, N=139), PDD-NOS (PDD, N=61), or typical development (TD, N=147). Diagnostic groups and individual growth curves

for HC, height, and weight were modeled using spline curves, with gender and gestational age as covariates. Principal components analysis (PCA) was applied to fitted HC, height, and weight curves, yielding PC curves as functions of age (see Chawarska et al, 2011). Features of PC curves were included in multivariate linear regression models to predict ADOS severity score and Verbal and Nonverbal DQ based on Mullen Scales at 36-48 months within subjects with ASD.

Results: 87% of the variance in the three morphological measures was explained by two principal components: generalized body overgrowth (PC1), and large head relative to body size (PC2). Increased PC1 at birth was associated with increased autism severity score (regression coefficient $\beta=0.35$, $p=0.027$), lower Verbal DQ ($\beta=-5.15$, $p=0.028$) and lower Nonverbal DQ ($\beta=-4.14$, $p=0.008$) at three years of age. Increased rate of growth in PC1 between birth and 24 months was associated with lower Verbal DQ ($\beta=-4.24$, $p=0.009$) and lower Nonverbal DQ ($\beta=-2.69$, $p=0.012$) at three years. PC2 at birth was negatively associated with autism severity score ($\beta=-0.78$, $p=0.025$), but neither PC2 at birth or rate of growth in PC2 had any significant effects on Verbal or Nonverbal DQ. Interaction effects between overgrowth features and gender were not significant, indicating that the relationships between overgrowth and phenotypic outcome were similar for boys and girls.

Conclusions: Larger **overall body size at birth** predicted increased autism severity symptoms and decreased verbal and nonverbal skills at age three. In addition, presence of *an accelerated rate of growth* of **overall body size** between birth and 24 months led to an additional decrease in both Verbal and Nonverbal DQ by the age of three years, above and beyond the effects seen at birth. These findings suggest that features of morphological growth may constitute useful biological predictors of developmental outcome in young children with ASD. However, the mechanisms underlying the relationship between overgrowth and clinical presentation remain to be investigated.

160.023 23 Neurodevelopmental Phenotype in Pitt-Hopkins Syndrome. I. D. van Balkom*¹ and R. C. Hennekam², (1)*Lentis Psychiatric Institute*, (2)*Academic Medical Center, University of Amsterdam*

Background: Pitt-Hopkins syndrome (PTHS) is characterized by intellectual disability, distinctive facial characteristics, breathing abnormalities, epilepsy and repetitive behaviors. It is caused by deletions/mutations in *Transcription Factor 4 (TCF4)* on chromosome 18 (18q21). Previous publications have primarily focused on genetic/somatic aspects.

Objectives: To study whether autism spectrum disorder (ASD) is part of PTHS neurodevelopmental phenotype.

Methods: Subjects with molecularly confirmed *TCF4* mutations were recruited through the Dutch PTHS Family Association (N=10). Participation of 4 girls and 6 boys was determined by proximity to research center, and availability within the study timeframe; median age was 10 years (range 3-24). All participants completed individual psychiatric and neuropsychological assessments, including Bayley Scales of Infant Development (BSID-II), Vineland Adaptive Behaviour Scales – Survey Form (VABS), and Developmental Behavior Checklist-Primary Carer (DBC-P) for ≤18 years and Adults (DBC-A) for those >18 years. 8 subjects completed the Autism Diagnostic Interview-revised (ADI-R).

Results: **Clinical psychiatric assessments (n=10)**. Most participants showed amiable demeanor, but had difficulties engaging socially. 9 had no speech or only single words. All participants made repetitive hand/finger movements, 9 repetitively fiddled with toys and showed a fascination with a (part of a) specific object. 6 participants repetitively played with the same toy or same activity (music, video). 6 participants had breathing abnormalities. Self injury was seen in 5, aggression in 4 participants. Parents of 5 participants noted difficulties with changes in daily routine. **BSID-II (n=10)**. All participants had severe intellectual disability. Chronological ages ranged from 32 to 289 months; the range of age equivalent scores for the mental scale was 3.5 to 15 months, and for the motor scale 4 to 19 months. **VABS (n=10)**. No participant, except the eldest, performed beyond a developmental age of 20 months. Adaptive functioning on the domains of daily living skills and communication appeared better than functioning on the socialization domain. Progress in adaptive functioning with age was

limited. **DBC (n=10)**. Two participants scored above the clinical cut-off for problem behaviors for age group (with elevated scores on Self-Absorbed, and Communication Disturbance/Disruptive Behaviour scales). All participants had high scores on self-absorption. Five of 7 subjects <18 years scored above threshold on DBC Autism Screening Algorithm. **ADI-R (n=8)**. Highest scores for all participants were found on the social interactions and play domains. All subjects scored ≥ cut-off scores on social and communication domains. Two participants did not score above cut-off for behavioral domain.

Conclusions: In this first study of neurodevelopment and behavior in PTHS all subjects shared a phenotype of (very) profound intellectual disability, severe impairments in social interaction, communication/language, and highly frequent, intense stereotyped behaviors. Psychiatric assessments additionally showed repetitive play, fascinations, and insistence on sameness. The quality and intensity of social, communication and behavioral difficulties in our sample are beyond what would be expected even for the very low cognitive level found and therefore cannot be readily explained by it. We conclude that the PTHS phenotype includes ASD in varying degrees of severity.

160.024 24 Testing the Boundaries of Autism Spectrum Disorder in DSM-5. W. Mandy*¹, T. Charman² and D. H. Skuse³,
(1)University College London, (2)Institute of Education,
(3)Institute of Child Health, UCL

Background: Diagnostic criteria for autism will be radically revised in the fifth edition of the DSM, published in 2013. Changes include the creation of a single unitary category of autism spectrum disorder; the replacement of the autism triad with an autism dyad; the removal of the Asperger's disorder and pervasive developmental disorder – not otherwise specified (PDD-NOS) diagnostic sub-categories; the inclusion of sensory abnormalities as a core ASD symptom; and the removal of language delay from diagnostic criteria. Empirical evidence already exists that these modifications will improve the reliability and validity of ASD. However, concerns have arisen that the threshold for receiving a diagnosis on the autism spectrum in DSM-5 is set too high; several studies have suggested that DSM-5 ASD criteria will exclude around 40% of those currently meeting DSM-IV-TR criteria; and that sensitivity

will be especially poor for high-functioning individuals. Proponents of DSM-5 have countered these claims, arguing that such research is flawed, as it used data that were collected to capture DSM-IV and DSM-III defined symptoms, and so failed to properly implement DSM-5 diagnostic criteria.

Objectives: Using detailed and comprehensive phenotyping, we aimed to accurately implement DSM-5 ASD criteria to test whether they exclude from the autism spectrum individuals with a DSM-IV Asperger's, autism or PDD-NOS diagnosis.

Methods: Participants were 726 verbally able (mean verbal IQ=91) children and young people (mean age=9.5 years) who had been referred to a clinic for the assessment of social communication difficulties. All either met DSM-IV-TR criteria for PDD, or had significant, sub-diagnostic autistic traits characteristic of the broad autism phenotype. Symptoms were assessed by parent report using the Dimensional, Diagnostic and Developmental Interview (3Di). This interview contains over 200 questions capturing the full range of autistic phenomena, well beyond those described in DSM-IV-TR criteria. 140 of these questions were combined to create a DSM-5 algorithm, which mapped the full range of symptoms described in DSM-5 ASD criteria.

Results: Of the children with a DSM-IV-TR PDD diagnosis, 86% met criteria for DSM-5 ASD. Of the 231 children without a DSM-IV-TR PDD diagnosis, 61 (26%) met criteria for DSM-5 ASD. Most cases of DSM-IV-TR autism (175 of 185; 95%) and Asperger's disorder (137 of 143; 96%) met DSM-5 criteria for ASD. Of the PDD-NOS cases 69% (115 of 167) met DSM-5 criteria for ASD. Of the 52 people with PDD-NOS who did not reach thresholds for ASD, 37 had insufficient repetitive behaviours for a DSM-5 diagnosis. Neither IQ nor age was associated with the risk of not meeting criteria for ASD.

Conclusions: Our findings contradict studies that have suggested severely reduced sensitivity of DSM-5 ASD criteria in higher-functioning individuals. We attribute this to our ability to use detailed phenotyping to accurately implement the full range of ASD symptoms described in DSM-5. Nevertheless, we identified a group of individuals who may miss an ASD diagnosis, due to

insufficient repetitive and stereotyped behaviour. We anticipate that their profile of difficulties will be captured by 'Social Communication Disorder', a new category that will appear in DSM-5.

160.025 25 Risk for Social Behavioral Problems and Autistic Traits in Children with an Extra X Chromosome. H. Swaab*, *Leiden University, Faculty of Social Sciences*

Background:

Approximately 1 in 700-1000 boys are born with an extra X chromosome, also known as Klinefelter syndrome (KS). Because of the risk for development of psychopathology such as autism spectrum disorders, it has been suggested that studying individuals with KS may help in the search for cognitive, neural and genetic mechanisms underlying autism symptoms.

Objectives:

It has remained unclear however, 1) to what extent girls with an extra X chromosome have an increased vulnerability for autism traits and 2) what the profile and severity is of autism traits as compared to children with autism spectrum disorders (ASD). This study will address this.

Methods:

In total, 60 children (35 boys and 25 girls) with an extra X chromosome, 60 boys and girls with ASD and 110 non-clinical controls participated in the study. The age range was 9 to 18 years. We used the Autism Diagnostic Interview-revised (ADI-R) to assess clinical symptoms of ASD. The Social Responsiveness Scale (SRS) and the Autism Questionnaire (AQ) were used to quantify autistic traits.

Results:

Data from the ADI-R showed that 28, 8% of the children with an extra X scored above the cut-off on all three domains: social interactions, communication and rigid or stereotyped behavior. Mean ADI-r scores were similar in boys and girls with an extra X chromosome. In line with this, scores on the SRS and AQ were significantly increased and in between those of controls and children with ASD. The effect size (Cohen's d) was 1.4, indicating that scores were 1.4 standard

deviations higher in the extra X group as compared to the control group. Scores were similar for boys and girls with an extra X.

Conclusions:

Our findings illustrate the profile of increased risk for autism symptoms in children with an extra X chromosome. This may help in diagnosis and treatment of children with an extra X. The absence of gender effects is not only relevant for clinical practice, but may also provide important clues with regard to role of the extra X chromosome in social development. Our findings of elevated levels of autistic traits in both boys and girls with an extra X, stress the relevance of studying X-linked mechanisms.

160.026 26 What about the Girls? Examination of Gender Differences in a University Wide ASD Sample. A. Vehorn^{*1}, A. S. Weitlauf¹, Z. Warren¹ and K. Gotham², (1)*Vanderbilt Kennedy Center*, (2)*Vanderbilt University*

Background: ASDs have long been thought to be more prevalent in males (Fombonne, 1999; Lingam et al., 2003), and the CDC currently estimates that males are five times more likely to have an ASD than females (CDC 2012). Attempts to describe sex differences within the disorder generally identify IQ as the main differentiating factor between the sexes, reporting that females were more likely to have intellectual disabilities than males with ASD (Wing, 1981; Tsai & Beisler, 1983; Lord & Schopler, 1987; Volkmar, Sparrow and Szatmari, 1993). More recent work with young children with ASD (Carter et al. 2007; Hartley & Sikora, 2009) suggests significant differences exist between the sexes in cognitive profiles but not in overall cognitive level. Ongoing changes to diagnostic labels and criteria, rising population prevalence estimates, and increased public awareness of ASD necessitate further clarification of potential sex differences in prevalence, cognitive and adaptive skills, and autism symptoms.

Objectives: To assess for sex differences in a sample of 1018 males ($M = 6.24 \pm 4.35$, range = 1.20-36.41) and 196 females ($M = 6.18 \pm 5.03$, range = 1.32-36.41), drawn from a university based clinical research database.

Methods: We examined possible differences between the sexes with regards to cognitive level, adaptive behavior (Vineland-II; Sparrow et al., 2005) and autism symptoms (Calibrated Severity Scores [CSS]; Gotham et al., 2009), collectively and after controlling for age, cognitive level and ADOS module (Lord et al., 2000).

Results: When the entire sample was analyzed, no significant sex differences were found in cognitive level ($t = -1.53$; $p = .127$), adaptive behavior ($t = -1.19$; $p = .234$), or autism severity ($t = -.851$; $p = .395$). When the sample was divided by age range, no significant differences emerged in males or females in the 0-2:11 or 3-5:11 age range. CSS scores were significantly higher for males in the 6-12:11 range ($p = .021$) and the 13-17:11 range ($p = .037$). No significant differences emerged in cognitive or adaptive level. When divided by cognitive level, no significant differences emerged in CSS or adaptive level. When divided by ADOS module, a significant difference emerged in CSS for Module 3 ($p = .047$), with males scoring significantly higher than females.

Conclusions: Contrary to the majority of research in the area, no significant differences in cognitive skills were found between the sexes. Based on differences in CSS, males presented with significantly higher autism symptomatology in the school age range and when assessed with a Module 3 ADOS. This raises the question of whether the difference in overall prevalence rates between males and females is related to true sex differences or if gender differences (i.e., culturally masculine vs. feminine traits) play a more significant role. Perhaps prevalence rates for school-aged females are artificially deflated, due to a milder symptom presentation or socio-cultural biases in assessment of autism symptomatology in females.

160.027 27 Identifying Autism Genes in Large Multiplex Families. N. J. Brown^{*1}, M. Bahlo², P. Lockhart³, L. Gordon⁴, T. Vick¹, C. Bromhead², P. Hickey², H. Mountford³, G. Gilles³, E. Fitzpatrick³, P. H. Hewson¹, M. Delatycki⁵, V. Anderson⁶, S. Wilson⁷ and I. E. Scheffer⁷, (1)*Barwon Health*, (2)*The Walter and Eliza Hall Institute of Medical Research*, (3)*Bruce Lefroy Centre for Genetic Health Research, MCRI*, (4)*Murdoch Childrens Research Institute*, (5)*Austin Health*, (6)*Royal Children's Hospital*, (7)*University of Melbourne*

Background: Autism spectrum disorders (ASD) are a group of neurodevelopmental disorders characterized by impairments in language, social interaction and repetitive or stereotyped behaviours. ASD has a strong genetic basis with heritability estimated at approximately 90% and up to 20% of relatives of individuals with ASD displaying the "broader autism phenotype" (BAP). Underlying genetic aetiology is heterogeneous, with the majority of cases remaining unsolved. Novel methodologies are required to disentangle the complex genetic architecture of these disorders.

Objectives: To clinically phenotype large families with multiple affected individuals with ASD and the BAP, and to map these families to identify novel ASD genes of major dominant effect via linkage analysis.

Methods: We phenotyped participants from large multiplex families using multiple standardized measures and a semi-structured interview including specific tasks to evaluate the BAP. Data was gathered regarding developmental, medical, psychiatric, vocational, and educational history, as well as hobbies and interpersonal relationships. Participants were formally evaluated for cognition, language skills, and executive function. A BAP rating system was developed to quantify specific BAP traits. Hierarchical cluster analysis of these BAP scores was used to identify phenotypic subgroups. Phenotypic patterns were scrutinized to determine affected status. Genotyping was performed and parametric linkage analysis conducted.

Results: We phenotyped 64 individuals from two large families and mapped ASD traits in both pedigrees. Five endophenotypic clusters of BAP traits were identified via hierarchical cluster analysis. Phenotypic patterns varied between families, with Family A demonstrating more individuals with disordered pragmatic language as their strongest feature, while aberrant social function was the most common endophenotype in Family B. In Family A we identified an 8Mb region suggestive of linkage at chr7q21.11-7q21.3 with a parametric LOD score of 2.76. Haplotype analysis demonstrated segregation with 15/17 affected individuals. In Family B we obtained a genome wide significant maximum LOD score of 3.3 for a

0.5Mb region at chr17p13.3. The critical haplotype was identified in 14/15 affected individuals.

Conclusions: We mapped ASD and BAP traits in two large multiplex families by employing novel methodology to identify the BAP. Phenotypes varied between the two families but phenotypic patterns showed intra-familial similarities, in keeping with the recognised phenotypic heterogeneity within ASD. Linkage data indicates a high probability that a causative mutation lies within the linkage region for each family. Next generation sequencing will be used to identify these variants. Gene identification will inform the neurobiology of ASD and could potentially lead to novel treatments.

160.028 28 Behaviour Problems Among School-Aged Children with ASD: Associations with Children's Communication Problems and Parenting Behaviours. H. Boonen*¹, J. P. W. Maljaars¹, G. Lambrechts², K. Van Leeuwen¹ and I. Noens¹, (1)University of Leuven (KU Leuven), (2)Parenting and Special Education Research Unit, University of Leuven (KU Leuven)

Background: Research has clearly demonstrated that behaviour problems are common in children with ASD (Hartley, Sikora, & McCoy, 2008; Kanne & Mazurek, 2011). These challenging behaviours can form an important source of stress for parents and often cause more distress to parents than the core ASD symptoms. Prior research indicated various risk and protective factors in predicting behaviour problems among typically developing children. Both child factors (e.g. child temperament) and contextual factors (e.g. parenting behaviours) seem to be associated with behaviour problems. Only a few studies have focused on exploring these risk and protective factors among children with ASD. Moreover, these studies have only investigated individual child factors, such as cognitive and language abilities (Dominick et al., 2006; Kanne & Mazurek, 2011). Hence, there is a need for research investigating child and contextual factors that are associated with behaviour problems among children with ASD.

Objectives: 1) to explore whether communication problems are associated with behaviour problems among children with ASD; 2) to examine if parenting behaviours mediate or moderate the relationship between behaviour problems and communication problems

Methods: Data were collected from 206 children with ASD and 189 children without ASD. All children were school-aged (ages 6 to 12). The Strengths and Difficulties Questionnaire was administered to evaluate behaviour problems. In the current study four subscales were used, creating two composite scores for internalizing behaviour problems (emotional and peer problems items) and externalizing behaviour problems (conduct and hyperactivity items). The Children's Communication Checklist-2 was used to measure communication problems. From this questionnaire eight subscales were used, creating two composite scores for structural language problems (speech production, syntax, semantics and coherence) and pragmatic problems (inappropriate initiation, stereotypic language, use of context and non-verbal communication). The Parental Behaviour Scale-short version (PBS; Van Leeuwen & Vermulst, 2010) was used to measure general parenting behaviours (Positive Parenting, Discipline, Harsh Punishment, Material Rewarding, and Rules). Two additional subscales were administered to measure parenting behaviours more specifically relevant to children with ASD (Stimulating the Development and Adapting the Environment; Van Leeuwen & Noens, 2010).

Results: Preliminary results indicate that both children's communication problems and parenting behaviours are associated with behaviour problems among children with ASD. Pragmatic problems are positively associated with both externalizing ($r = .25, p < .001$) and internalizing behaviour problems ($r = .37, p < .001$), while structural language problems are only associated with internalizing behaviour problems ($r = .14, p < .05$). With regard to parenting behaviours, externalizing behaviour problems are positively associated with rules ($r = .14, p < .05$) and punishment ($r = .28, p < .001$), whereas internalizing problems are positively associated with stimulating the development ($r = .18, p < .01$) and adapting the environment ($r = .27, p < .001$).

Conclusions: In these preliminary analyses, we only looked at correlation patterns in the ASD group. In further analyses, hierarchical regression analyses will be performed in order to explore whether these associations differ in the control group and to examine if parenting behaviours

mediate or moderate the relationship between behaviour problems and communication problems.

160.029 29 Increased Heartbeat Interoception Is Predicted by Autism Spectrum Traits in the Typical Population. N. David*¹, R. T. Azevedo², B. Lenggenhager³, S. M. Aglioti² and I. Minio-Paluello², (1)University Medical-Center Hamburg Eppendorf, (2)Sapienza Università di Roma, (3)University Hospital of Child and Adolescent Psychiatry

Background: The term interoception describes the sensitivity to or awareness of internal bodily processes such as arising from the heart or visceral organs. Interoceptive awareness has been proposed as fundamental building block of self-awareness, emotions, decision making and empathy. Decreased interoception has been associated with alexithymia, which is characterized by difficulties in processing one's own emotions. Although impairments in, for example, self-referential and affective processing as well as empathy have been described for Autism Spectrum Disorders (ASD), the link to a fundamental deficit in interoception has not been made yet.

Objectives: We sought to investigate the relationship between interoceptive awareness and autistic traits, empathetic concern, perspective taking, and alexithymia in the typical population.

Methods: A classical heartbeat counting task was used to measure cardiac awareness as one type of interoception in 37 typically developed adults. Participants were asked to introspect and count their own heartbeat. The extent to which typical adults displayed autistic traits was measured using the autism-spectrum quotient (AQ). Moreover, empathetic concern and perspective taking were assessed with the Interpersonal Reactivity Index (IRI) and Alexithymia with the Toronto Alexithymia Scale (TAS-20).

Results: Heartbeat counting was positively correlated with the overall extent of autistic traits on the AQ. That is, the more accurate the participants' ability to count their own heartbeat, the more autistic traits they reported. There was no other correlation with cardiac awareness but perspective taking correlated negatively with the "communication" subscale of the AQ (i.e., self-

reported use of language in a social context). In addition, difficulties describing feelings on the TAS correlated positively with "attention to detail" and "social skills" subscales of the AQ as well as with empathetic concern on the IRI.

Conclusions: In contrast to previous assumptions, higher autistic traits are not associated with low interoceptive sensitivity but the opposite: typical adults with high AQ scores showed higher cardiac awareness. Instead of a deficit, higher egocentrism in ASD or typically developed adults with high AQ scores could represent an advantage for interoception. The present result contributes to the present discussion whether the self in ASD is best characterized as absent or as all too present.

160.030 30 Autism Symptomatology in Males with Chromosomal Aneuploidies: A Comparison with Idiopathic Autism. N. R. Lee*¹, A. C. Sharber², L. S. Clasen¹, D. Fidler³, S. Hepburn⁴, C. Robinson⁴, L. Kenworthy², J. Giedd¹ and G. L. Wallace¹, (1)*National Institute of Mental Health*, (2)*Children's National Medical Center*, (3)*Colorado State University*, (4)*University of Colorado*

Background:

Autism is defined by impairments in reciprocal social interaction (SOC), communication (COM) and repetitive/restrictive interests and behaviors (RBI). Of late, there has been a suggestion in the literature that components of the ASD phenotype are dissociable and that each may be attributed to differing etiological, neuropsychological, and neurobiological underpinnings. In a parallel line of investigation, there has been an increased interest in characterizing ASD symptom profiles (or rates of comorbid ASD) in individuals with different genetic syndromes associated with intellectual disability. Examining symptom profiles across disorders of known genetic etiology may elucidate mechanisms contributing to the development and fractionation of the ASD phenotype.

Objectives:

We sought to examine ASD symptom profiles using the Social Communication Questionnaire – Revised, Lifetime Version (SCQ) in males with four chromosomal aneuploidies associated with intellectual deficits (XXXY, XYY, XXXY, Down syndrome [DS]) and to compare these profiles to

that found for a clinically-ascertained group of children with idiopathic ASD.

Methods:

Ninety-six males, ages 4-30 years, participated (ASD:n=38, XYY:n=28, XYY:n=7, XXXY:n=14, DS:n=9). The mean age of the sample was 11.60±5.65 and the mean verbal IQ was 71.26±14.54. Participants were a subset of individuals enrolled in studies at the NIMH, Children's National Medical Center, and University of Colorado Medical School.

For data analyses, SCQ total scores were compared among four groups (ASD, XYY, DS, and a combined XYY/XXXY group). Next, the proportion of autism-positive responses on SCQ items in each subdomain (SOC,COM,RBI) was calculated (i.e., # autism-positive responses/# of items in subdomain). This was done so that subdomain scores which include different numbers of items could be compared directly.

Results:

SCQ total and subdomain scores were examined non-parametrically using Kruskal-Wallis tests. For SCQ total and subdomain scores, there were significant effects of group (all X^2 s>12, all $ps<.01$). Follow-up Mann-Whitney tests revealed that the ASD group had greater SCQ total scores than the combined XYY/XXXY and DS groups ($ps<.05$ Bonferroni-corrected), but not the XYY group. For the subdomain scores, the pattern was SOC: ASD>XYY/XXXY,DS; COM: ASD>all groups; RBI: ASD>XYY/XXXY,XYY. To examine disorder-specific profiles, within-group subdomain comparisons were completed utilizing Friedman tests. No significant differences between subdomain scores were detected within the XYY, XYY/XXXY, and ASD groups. Rather, SCQ profiles were flat. For the DS group, SOC was marginally less impaired than both COM and RBI ($p<.05$ uncorrected).

Conclusions:

This research contributes to the growing literature on ASD profiles in genetic disorders. The pattern of findings varied when examining SCQ total versus subdomain scores. The ASD group was

more impaired than the combined XXXY/XXXXY group for all scores. In contrast, the ASD group had greater COM and RBI symptom endorsement scores than the XYY group, but did not differ on total and SOC scores. Finally, the ASD group was more impaired than the DS group on all scores except RBI. This research suggests that examining SCQ subdomains may be more informative when characterizing ASD symptomatology in children with genetic disorders. Additionally, studying these subdomains in groups with distinct genetic syndromes may elucidate mechanisms underlying the fractionable ASD phenotype.

160.031 31 Association Between SSRI Exposure During Pregnancy with Behaviors and Conditions Among Children with ASD. R. A. Harrington^{*1}, L. C. Lee¹, R. M. Crum¹, A. W. Zimmerman² and I. Hertz-Picciotto³, (1)*Johns Hopkins Bloomberg School of Public Health*, (2)*Lurie Center/MGH*, (3)*University of California at Davis*

Background: ASDs are heterogeneous disorders that have numerous etiologies, making risk factor identification difficult. Case-group stratification may help researchers identify more homogeneous subgroups that would aid in the assessment of causal mechanisms for ASD. Different symptom profiles or behaviors among children with ASD who were or were not prenatally exposed to selective serotonin reuptake inhibitors (SSRIs) could indicate a potential role of serotonin in ASD development among some children.

Objectives: To examine associations between prenatal SSRI exposure and the occurrence of developmental and behavioral characteristics, as well as clinical features, in a population-based sample of young children with confirmed ASD.

Methods: Cases of ASD from the Childhood Autism Risks from Genetics and the Environment (CHARGE) study, a large population-based case-control study, were analyzed to evaluate differences between those who were and were not prenatally exposed to SSRIs. Children were assessed on the ADOS, ADI-R, Vineland Adaptive Behavior Scales (VABS), and Mullen Scales of Early Learning (MSEL). Questionnaires collected extensive comorbidity and medication data for both the mother and child. Mother-child pairs for which self-reported maternal medication history was available totaled 492 children with ASD, 29 exposed and 463 unexposed. Exposure was defined as mothers who reported taking an SSRI

between conception and birth. Multivariate linear and logistic regression models were used to assess the relationship between SSRI exposure during pregnancy and child characteristics.

Results: Cognitive functioning and adaptive behaviors were below average overall, but there was a tendency for exposed children to have higher scores. Generally, exposed children had a greater percentage of co-occurring clinical symptoms than did unexposed children. In multivariate analyses that adjusted for child's age, maternal age at child's birth, and maternal birthplace, SSRI exposed children had significantly higher overall MSEL composite scores (β : 6.64; 95% CI: 0.02, 13.26; +0.44 SDs) and VABS communication scores (β : 6.06; 95% CI: 0.51, 11.61; +0.40 SDs), suggesting better cognitive and adaptive communication functioning. In nonverbal children, communication scores were significantly lower as measured by the ADI-R (β : -1.32; 95% CI: -2.50, -0.14; -0.55 SDs), indicating less abnormality. Stereotyped/repetitive behaviors were significantly less abnormal in exposed children on the ADOS (β : -0.88; 95% CI: -1.51, -0.25; -0.24 SDs). The likelihood of having frequent gastrointestinal symptoms was higher in children exposed to SSRIs (AOR: 2.40; 95% CI: 1.05, 5.50), as were the odds of using over-the-counter or prescription medications indicated for any of the following: allergy, the central nervous system, gastrointestinal, or respiratory problems (AOR: 3.49; 95% CI: 1.50, 8.11).

Conclusions: Children with ASD who were prenatally exposed to SSRIs had better cognitive functioning, as well as less abnormal communication and stereotyped behaviors relative to unexposed children with ASD. GI symptom frequency and medication use were higher in exposed children. Unexplored familial socioeconomic characteristics may have confounding effects on these results. Future studies addressing how prenatal SSRI exposure affects serotonin levels and the functioning of the serotonergic system in a developing child would be invaluable to help understand what may be underlying these findings, and may point to potential etiologic mechanisms for ASD.

160.032 32 Comparison of Behavioral Development and Socio-Demographics Between Infants and Young Children At

Background: ASD is an inheritable condition and infants who have older siblings with ASD are at increased risk of ASD or autistic-like behaviors. Recent research has begun to identify early signs of ASD in at-risk infants. These studies have identified behavioural and developmental differences between at-risk infants subsequently diagnosed with ASD from at-risk infants not diagnosed, as well as between at-risk and low-risk infants. More research is needed on examining possible differences between at- and low-risk infants not just on core ASD symptoms, but also on collateral behaviors commonly seen in young children with ASD. There is also a need to determine if there are socio-demographic differences in at- and low-risk groups and if these demographic differences are related to early signs scores.

Objectives: (1) Determine if young children who have older siblings with ASD (at-risk group) have higher scores and more elevated items on a validated parent report measure of early signs of ASD than sex and age-matched children who have no family history of ASD (low-risk group); (2) determine if any socio-demographic differences exist between these two groups and (3) determine if socio-demographic differences are related to scores on the early markers scale.

Methods: This cross sectional study used the 61-item Parent Observation of Early Markers Scale (POEMS) to compare behavioral development of 69, 6-36 month old children at risk for ASD (older sibling diagnosed with ASD) to 69 sex and age-matched children with low risk (no family history of ASD). This parent-report, 4-point rating scale has been shown to have acceptable psychometric properties, sensitivity and specificity, when administered prospectively. It identified infant sibs who were subsequently diagnosed with ASD by 36 months from those who were not as early as 9 months of age.

Results: The at-risk children had significantly more elevated POEMS items (score of 3 or higher) than the low-risk children at 12, 18, 24, 30 and 36 months of age, even when seven subsequently diagnosed children (all in the at-risk group) were removed from the analyses. Differences were

noted in core social-communication skills (e.g., imitation, interest in faces) as well as behavioral challenges commonly seen in older children with ASD (e.g., sleep issues, intolerance to waiting). POEMS total scores were not significantly different. Families of high risk children had older parents, lower family incomes and fewer mothers working out of home. These socio-demographic variables were not significantly correlated with POEMS scores.

Conclusions: The results support the use of the POEMS as a prospective parent report measure to monitor possible early signs of ASD and collateral behaviors associated with the broader phenotype. The study highlights the need to examine elevated items (as opposed to just total scores), and to include subsidiary behaviors and socio-demographic data in comparison studies. Future research will examine developmental trajectories of at-risk infants in longitudinal studies using the POEMS.

160.033 33 Does WISC-IV Underestimate the Intelligence of Autistic Children?. A. M. Nader*¹, V. Courchesne², I. Soulières¹ and M. Dawson², (1)*University of Quebec in Montreal*, (2)*Centre d'excellence en Troubles envahissants du développement de l'Université de Montréal (CETEDUM)*

Background: Wechsler Intelligence Scale for Children (WISC) remains a widely used measure of intellectual functioning in autism. However, previous findings comparing autistic performance on WISC-III versus Raven's Progressive Matrices (RPM) suggest that while both tests provide similar estimates of nonautistic intelligence, autistics perform significantly, and sometimes dramatically, better on RPM. Furthermore, in contrast to autistic children's uneven WISC-III subtest profile, item by item RPM performance in autistics and nonautistics is highly correlated. These results suggest that RPM, a durable and important marker of fluid intelligence, better represents autistic intelligence than does Wechsler FSIQ. WISC-IV, released in 2004, introduced significant changes in Wechsler subtests and in the structure of different index scores. Indeed, the new perceptual reasoning index (PRI) has only one timed visuo-motor subtest and includes the new Matrix Reasoning subtest, which is similar to some aspects of RPM.

Objectives: We aimed to determine whether the latest WISC version continues to underestimate autistic intelligence.

Methods: 26 autistic and 22 typically developing children (age 6-16 years) completed WISC-IV and RPM at two different times. Levels of performance were compared through inspecting percentiles derived from mean standard scores (WISC-IV) and from mean raw scores and ages (RPM) for each group. Parametric and nonparametric statistical comparisons were then conducted with individual percentiles. Similar results were obtained with all procedures.

Results: Typical children achieved similar percentile values on RPM (73rd percentile) and WISC-IV FSIQ (75th percentile). This was not the case for autistic children, who scored at the 61st percentile on RPM but only at the 21st percentile on WISC-IV. A significant difference between RPM and WISC-IV scores was found in the autistic group ($p < .0005$ in both parametric and nonparametric tests) but not in the typical group ($p = .57$ in parametric and $p = .67$ in nonparametric tests). In line with these results, the advantage of RPM over WISC-IV FSIQ was significantly greater for autistic than for typical children. Five autistic children, but no typical children, obtained RPM scores over 50 percentile points higher than their WISC-IV scores. While three autistic children had standard scores below 70 on WISC-IV, the lowest autistic RPM score was at the 10th percentile (IQ-equivalent estimate 81). The rest of the autistic children achieved RPM percentile scores of 18 or higher, with estimated RPM IQ-equivalents over 85. With respect to WISC-IV index scores, autistic children attained a mean Verbal Comprehension Index standard score of 84.6, compared to a mean PRI score of 104, which in turn was similar to their estimated RPM IQ-equivalent score.

Conclusions: Our results are consistent with and add to existing findings that Wechsler FSIQ significantly underestimates autistic intelligence. Given what is known about RPM as a complex test of fluid and general intelligence, our results also further challenge the notion that autistic strengths are at best a collection of simple, isolated, and low-level perceptual abilities. Finally, our results provide preliminary evidence that the WISC-IV PRI index score may better estimate autistic intelligence than WISC-IV FSIQ. These findings

merit attention in both research and clinical practice.

160.034 34 Social/Emotional Functioning in Optimal Outcome Children with a History of Autism Spectrum Disorders. D. A. Fein*, K. E. Tyson, M. Barton, I. M. Eigsti, L. Naigles, E. Troyb, A. Orinstein and M. Helt, *University of Connecticut*

Background: Although ASD's are usually considered a life-long set of disorders, and are so for the majority, a number of such individuals can lose symptoms and gain skills so that they no longer meet criteria for any ASD. The present paper is part of a larger project in which a group of such individuals are being studied in multiple domains, including neuropsychological, psychiatric, and social functioning, and brain structure and function. The goal is to document the possibility of an outcome of ASD in which social and cognitive functioning is typical, to examine any residual vulnerabilities, and to explore mechanisms of "optimal outcome" by tracking history, intervention and structural and functional imaging differences from individuals with persisting ASD.

Objectives: The aim of this paper is to present findings on social and emotional functioning, including adaptive social and communication scores, ADOS scores, face recognition, and psychiatric vulnerabilities.

Methods: Participants were 44 individuals with high-functioning autism (HFA), 34 individuals with optimal outcome (OO), and 34 individuals with typical development (TD). Age range was 8-21, with an average age of 13 years in all groups. All participants had verbal IQ, performance IQ and full-scale IQ in the normal range (>77). HFA participants met criteria for an ASD on the ADOS and by best estimate clinical judgment. OO participants did not meet criteria for an ASD on any ADOS domain or by clinical judgment, were functioning in a regular education classroom with no one-on-one assistance and no special services for social skills, had Vineland Communication and Socialization scores in the normal range, and had an early history of ASD supported by early expert diagnosis and current blind review of early records.

Results: ADOS Social and Communication totals did not differ between OO and TD groups. One social item (insight into relationships) was

significantly higher (more abnormal) in the OO than the TD group, and one item showed a trend (eye contact). No Communication items differed between OO and TD groups. The Social Communication Questionnaire Lifetime Version suggested that the OO group had slightly milder clinical presentation in early childhood and the ADI-R suggested that this difference was only in the social domain. Facial Recognition score was average for the OO group and not significantly different from the TD group, while the HFA group's average score was below average. The OO group did not differ from the TD group on any Vineland domain. Both the OO and HFA groups were vulnerable to current and past attention problems and specific phobias, with the HFA group also vulnerable to depression, tics, obsessive-compulsive disorder, and oppositional-defiant disorder.

Conclusions: Data support the existence of a group of individuals with a clear history of ASD and outcome in the normal range of social functioning and communication. They are vulnerable to attention difficulties and phobias, and appear to have had slightly milder social deficits in early childhood.

160.035 35 Characteristics of Children Who Lost an Autism Diagnosis: A Sample From Istanbul, Turkey. N. M. Mukaddes*¹ and D. Tutkunkardas², (1)*Istanbul University, Istanbul Faculty of Medicine*, (2)*Istanbul University*

Background: Although follow up studies on individuals with diagnosis of autism spectrum disorders show that the out come is not favorable in this group, scattered evidence suggests a loss of diagnosis in 3-25% of individuals with autism spectrum disorders.

Objectives: The aim of this study is to describe a group of children who moved off the autism spectrum following intensive educational programming.

Methods: The method is descriptive, reporting the characteristics of the children (n: 41) and explaining their educational programs. The data were collected by reviewing participants' files.

Results: All the children had regular psychiatric follow-up. The mean age at referral was

2.35±0.75 years and mean age when diagnosis was lost was 5.00±1.97. Thirty-nine of them received the diagnosis of Autistic Disorder and two received the diagnosis of PDD-NOS according to DSM-IV-TR. Four of them (n: 41) were in early intensive behavioral intervention (EIBI), and the rest were in a comprehensive-eclectic educational program mostly provided by parents under supervision of educators. The Childhood Autism Rating Scale (CARS) total score at baseline was 32.54±2.74 and at final evaluation was 17.93±1.77. Mean IQ at final examination was 113.78±19.36.

Conclusions: It can be concluded that some children with ASD who received early intervention can move off the autism spectrum. The young age at intake, potentially high IQ, relatively mild symptoms, and intensive early education program may be important factors contributing to this positive outcome.

160.036 36 Growth Dysregulation in Boys with Autism Spectrum Disorder. C. Green*¹, C. Dissanayake² and D. Loesch², (1)*School of Psychological Science, La Trobe University*, (2)*La Trobe University*

Background: Head circumference growth in individuals with an Autism Spectrum Disorder (ASD) has been well characterised in the first two to three years of life, and reflects a period of acceleration followed by a period of deceleration when compared to typically developing (TD) peers. While this altered growth trajectory has been consistently found for head circumference, it is less clear if an abnormal growth trajectory also exists across measures of height and weight.

Objectives: The current study aimed to confirm the hypothesis that physical growth *overall* is dysregulated in ASD. Two explanatory hypotheses were tested: 1) a dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis, which regulates growth hormones; and 2) a connective tissue disorder, which is frequently associated with increased height and disproportionate body ratios.

Methods: The current study investigated growth patterns in 168 boys with an ASD and 875 TD boys from birth through 16 years of age using a mixed-longitudinal design.

Results: Although male infants with ASD were found to be smaller in size at birth compared to TD male infants, they grew at a significantly faster rate throughout infancy and toddlerhood. Once boys with ASD reached 4 years of age, they were significantly larger than TD boys, and remained so throughout childhood and adolescence, despite no longer differing in their rate of growth. There were significantly more boys with ASD who displayed extreme general overgrowth (measures in the 90th percentile for their age in height, weight, and HC) compared to TD boys.

Boys with ASD had longer limb to body ratios than TD boys; this, coupled with the increased height in the ASD group indicates possible involvement of the connective tissue in general growth dysregulation. There was a trend for the ASD group to have a lower 2nd to 4th digit ratio (an index of prenatal testosterone levels), indicating possible dysregulation of the HPA axis. Moreover, severity of ASD was highly correlated with an increase in the cortisol awakening response (CAR), an indicator of HPA axis function; however, there was no association between the CAR and specific growth patterns.

The boys with ASD who exhibited extreme general overgrowth did not differ from the other boys with ASD in any way to indicate the presence of a connective tissue disorder or HPA axis dysregulation in this small subgroup. However, they were significantly more affected as indicated by increased ASD severity in the extreme overgrowth group.

Conclusions: These findings implicate a general growth dysregulation in ASD from birth through adolescence, which may be due, in part, to a connective tissue disorder. Thus, an increased growth rate in early development may serve as a biomarker for a form of ASD. The discovery of a specific growth anomaly and its possible determinant(s) in ASD contributes to understanding the underlying mechanisms involved in the development of these related disorders, and warrants further investigation, especially of those children with ASD who exhibit extreme general overgrowth.

160.037 37 Understanding Women On the Autism Spectrum: Clinical Profiles of 70 Women with Mild ASDs. L. J. Burke*, K. P. Stoddart and S. Abdelsayed, *The Redpath Centre*

Background:

Recent literature suggests that women on the autism spectrum may be under-diagnosed. Anecdotal information has identified features that may present differently in women than in men, and a small number of studies have reported the presence of conditions which appear to co-occur in women on the spectrum at higher levels than expected, such as eating disorders. However, there is little research available to assist practitioners to better recognize ASDs in women.

Objectives:

To examine the profiles of women on the milder end of the autism spectrum in order to better identify characteristics that may provide a clearer profile of these women.

Methods:

The clinical files of 70 women on the milder end of the autism spectrum were reviewed. The women ranged in age from 18 to 68 years. These women were seen at a private practice which specializes in those on the autism spectrum, and particularly those at the milder end of the spectrum. All of the women were referred to the first author for a psychological assessment, and for most, the first diagnosis of Asperger syndrome or autism (high functioning). Variables of interest to the study were identified prior to the file review and each file was reviewed and variables coded. The data was analyzed using SPSS.

Results:

Among the results of interest, it was identified that a large proportion of women had family members on the autism spectrum, and of the women who had children, half of those children had a diagnosis of an ASD. A third of the women were in, or had been in a spousal relationship. Adaptive measures identified social skills which were well below expectations and many women had poor overall life skills functioning. Many had been diagnosed with related disorders prior to their ASD diagnosis, or had a diagnosis concurrent to the ASD. Over half the women experienced depression and three quarters, anxiety. Other diagnoses included specific learning disorder,

ADHD, eating disorder, OCD, sleep disorder, social phobia, panic disorder, adjustment disorder, Tourette’s disorder, bipolar disorder, attachment disorder and psychosis. All of the women reported sensory processing issues, and more than three quarters, motor planning concerns. The primary concurrent physical disorders were respiratory and gastrointestinal. Behavioral manifestations included inappropriate social responses, withdrawal, self-harm, aggression, rage and hoarding. Half the women reported alexithymia. While half of the women had high average to superior cognitive functioning and a third had completed a university/college program, one third women were unemployed and relied on family financially.

Conclusions:

The current study provides evidence of an emerging profile by which professionals can better understand women on the milder end of the autism spectrum and which will provide new avenues for investigation and support.

160.038 38 "the Evolution of Clinical Phenotyping in Post-Mortem Brain Tissue Research: Summary of Progress and Challenges". C. K. Hare* and J. Pickett, *Autism Speaks*

"The Evolution of Clinical Phenotyping in Post-Mortem Brain Tissue Research: Summary of Progress and Challenges"

Background:

A major aim of the Autism Speaks Autism Tissue Program when it started in 1998 was to provide research-relevant clinical information on brain donors with autism spectrum disorders. At that time, brain bank programs focused on the characterization and preservation of post-mortem brain tissue while little attention was paid to standardizing essential phenotypic and

clinical data. As additional post-mortem tissue resources are currently being developed in the US and Europe, there is a mounting sense of urgency in establishing exemplary standards. Such standards of clinical phenotyping would grant context and standardization to these rare resources and help facilitate a greater understanding of the tissue by the researchers that access them.

Objectives:

The purpose of this study is to explore existing clinical standards and protocols in post-mortem brain tissue research and communicate the evolution of the Autism Tissue Program’s Clinical Standard Operating Procedures. This exploration is conducted in consideration of: provision of pertinent phenotypic and clinical information to researchers and collection of phenotypic and clinical data from families while providing essential bereavement support.

Methods:

Review discussion and recommendations made for post-mortem clinical phenotyping via the ATP’s International Post-Mortem Brain Tissue Clinical Workgroup, including survey results of Principal Investigators. Consider Workgroup discussion and recommendations as well as advances in various clinical assessments to determine whether current ATP Clinical Protocols should be revised to maintain exemplary standards of phenotyping in post-mortem brain tissue research.

Results:

As a result of discussion amongst the members of the Clinical Workgroup, it is evident that any modifications to clinical protocol need to be made with tremendous consideration of the additional burden and potential fatigue of donor families. A survey of Principal Investigator’s prioritization of clinical data points was administered and yielded the following results (many of these points are addressed within the current ATP protocol):

| Clinical Data Points | Usefulness (2=required, 1=somewhat useful, 0=not useful) |
|--|---|
| ADI-R validation of Autism and domain scores | 2 |
| ADI-R raw data | .66* |

| | |
|---|-----|
| description of agonal state | 1 |
| seizure disorder | 2 |
| anxiety | 1 |
| GI Issues | 1.6 |
| ADHD | 1.3 |
| regression | 2* |
| aggression (classification and detailed description of) | 1.6 |
| sensory issues | 1.3 |
| repetitive behaviors | 1.3 |
| parental genotype/phenotype when available | 1 |

Conclusions:

1. The Autism Tissue Program Modified its Post-Mortem Clinical Standard Operating Procedures in 2012 to include the use of the CBCL, ACBL and SRS2. These measures were added to screen for data points not currently addressed by the ATP protocol and to minimize respondent fatigue. The ATP should consider the addition of a seizure survey.
2. Due to the low response rate conflicting results* of this survey, ongoing and broader dialogue is required between researchers and clinicians to increase potential for translational science to occur. This dialogue should be focused on informing clinicians to improve the relevance of clinical data collection; likewise clinicians can encourage greater use of the clinical data that already exists.
3. Ongoing dialogue is required across post-mortem brain tissue programs. This dialogue should be focused on improving upon existing processes in an effort to

provide researchers with gold-standard phenotypic and clinical data.

160.039 39 Behavioral Differences Across Sensory Processing Subtypes in Children Ages 6-10 with and without Autism. K. J. Tanner*, B. Hand and A. E. Lane, *The Ohio State University*

Background: Previous literature has determined that there is an association between sensory processing difficulties and challenging behaviors in children with autism; specifically, restricted and repetitive behaviors (Chen et al., 2009), stereotyped movements (Gal et al., 2010), and maladaptive behaviors (Lane et al, 2010).

Studies to date, however, have not examined the relative contribution of sensory processing difficulties to variance in challenging behaviors over and above that explained by autism diagnosis alone. Our lab has identified four sensory processing subtypes using the Short Sensory Profile (SSP): 1) no sensory impairment (NSI), 2) taste/smell sensitivity (TSS), 3) postural inattentive (PI), and 4) generalized sensory dysfunction (GSD). The subtypes are distinct in the sensory modality affected and in the severity of symptoms. By examining behavior patterns across sensory subtypes we can determine the relative usefulness of sensory features in describing patterns of general behavior when compared to knowledge of autism diagnosis.

Objectives: The purposes of this study were: 1) to better understand the relationship between patterns of sensory responding and general patterns of behavior in children with and without autism, and 2) to compare behavioral differences by sensory subtypes with those by diagnosis.

Methods: Participants (n=43) were children ages 6-10; 27 were typically developing and 16 were diagnosed with autism. Each participant was assigned to a sensory subtype using model-based cluster analysis of SSP scores (Lane et al, 2010; 2011). The Nisonger Child Behavior Rating Form (NCBRF) was used to assess each participant's general behavior, including both problem behavior and positive social behavior.

Results: Preliminary two-way ANOVA revealed significant differences in problem behaviors between subtypes (p=.001) regardless of diagnosis (p=.170). Mean problem behavior scores increased progressively from NSI (fewest

sensory symptoms, least problem behaviors) through GSD (most sensory symptoms, most problem behaviors). Post-hoc pairwise comparison with Tukey correction indicated significant differences between NSI and all other clusters, as well as between GSD and all other clusters. There were no significant differences on problem behaviors between PI and TSS. Two-way ANOVA examining positive social behavior scores revealed no significant difference for subtype ($p=.070$) and a marginal result for autism diagnosis ($p=.052$).

Conclusions: The findings of our study suggest that that sensory subtype may provide additional description of problem behavior patterns in autism than diagnosis alone. We found a clear relationship between sensory subtype and severity of problem behaviors. However, diagnosis of autism may be a better indicator of the presence of positive social behaviors than sensory subtype. The results of this study provide additional evidence for the utility of sensory features as a means of reducing heterogeneity in autism. One limitation of this study is its small sample size prohibiting the analysis of the relationship between sensory subtypes and specific forms of problem behavior.

160.040 40 Developmental Functioning and Medical Co-Morbidity Profile of Children with Complex and Essential Autism. J. Bellando^{*1}, J. Flor¹ and M. Lopez², (1)University of Arkansas for Medical Sciences, (2)Dennis Development Center

Background:

Using the Autism Dymorphology Measure (ADM), children with Autism Spectrum Disorders (ASD) may be categorized into either "complex" or "essential" autism. Individuals with complex autism are differentiated from essential autism by the presence of microcephaly and/or dymorphology. Previous studies with moderate sample sizes have found differences between complex and essential autism for certain developmental and medical markers. The complex subgroup was found to have lower IQ scores, poorer response to behavioral intervention, more seizures, and more abnormal EEGs and brain MRIs compared to the essential subgroup.

Objectives: The objective of this study is to determine if there are differences in complex vs. essential subjects based on developmental profile

(cognitive level, adaptive behavior, autism severity, quality of life, and behavioral ratings) as well as medical comorbidities (GI symptomatology, sleep problems and medication usage) that have been associated with ASD, in a larger cohort of subjects with well-defined ASD.

Methods:

This study utilizes data from 1,347 individuals (2-17 years old) enrolled in Autism Treatment Network (ATN) Registry. ASD diagnosis was established based on DSM-IV criteria and a standardized battery of assessments, which includes an Autism Diagnostic Observation Schedule (ADOS) and a medical evaluation. The ADM was used by trained physicians to classify subjects as complex or essential. Comparisons between complex versus essential for cognitive level, adaptive behavior, autism severity, quality of life, and behavioral ratings were assessed. Comparisons between the two groups for GI issues, sleep problems, and number of medications were also evaluated.

Results: The sample was homogenous in age and gender. 5.6% of the sample were classified as complex, with complex subjects more likely to have an Autistic Disorder diagnosis vs. Asperger ($p<.021$). For the developmental profile, significantly lower scores are seen for complex subjects in cognitive level ($p<.025$), adaptive behavior ($p<.001$), quality of life ($p<.050$). No significant differences in behavioral ratings or ADOS calibrated autism severity scores were found. For the medical comorbidities, complex subjects showed significantly increased physician-documented GI symptoms ($p<.003$), and are on higher number of medications ($p<.001$). No significant differences were found in parent-reported sleep problems.

Conclusions:

Using a large ASD sample, this study shows that complex and essential autism have distinct developmental and medical correlates, and thus underlines the importance of looking for dymorphology, even minor features, in the evaluation of a child with autism. Determining this distinction in autism may have implications in prognosis, identifying medical co-morbidities,

directing diagnostic evaluations, recommending treatment interventions, and future research participation.

160.041 41 Joint Attention and Social-Communicative Abilities of Siblings of Children with ASD. E. Demurie*, P. Warreyn, I. Schietecatte, N. L. Dewaele, M. Dereu and H. Roeyers, *Ghent University*

Background: Research on the broader autism phenotype (BAP) can benefit from studying early social and communicative skills of younger siblings of children with an autism spectrum disorder (ASD) (Tager-Flusberg, 2010). These siblings have a 10 to 20 times higher risk of developing ASD themselves and they are likely to share some behavioural characteristics with their older sibling (Szatmari, Zweigenbaum, & Bryson, 2004).

Objectives: High-risk siblings of children with ASD were followed between the ages of 7 and 36 months. For the current study, we focused on the ages of 12 and 18 months. Joint attention, language, and cognitive ability were investigated in both the siblings and a low-risk control group. Three research questions were formulated. First, do high-risk siblings show a generalized impairment in joint attention abilities as a component of the BAP? Second, can joint attention be an early marker for a later diagnosis of ASD in high-risk siblings? And third, can early joint attention predict the development of later language and cognitive abilities in both high-risk siblings and low-risk control children?

Methods: 33 infant siblings of children with ASD (of whom 6 with an ASD diagnosis at the age of 3) and 32 typically developing infants participated. At the age of 12 months, two aspects of joint attention were measured: initiation of joint attention (IJA) and response to joint attention (RJA), as well as cognitive ability with the Mullen Scales of Early Learning. At 18 months the joint attention measures were repeated, together with parent report on the M-CHAT and the Dutch version of the CDI. At 18 months the ADOS was administered as well.

Results: Unaffected siblings and typically developing children did not differ with regard to joint attention ability at both ages: both groups showed the same degree of IJA and RJA. However, siblings with a later ASD diagnosis had lower

scores than unaffected siblings for both IJA and RJA. Furthermore, in the combined sibling group, RJA at 12 months was predictive of ADOS and M-CHAT scores at 18 months. Furthermore, developmental index at 12 months was predictive of the social interaction score on the ADOS, M-CHAT and receptive language at 18 months. In the control group RJA only predicted the social interaction score on the ADOS.

Conclusions: Unaffected siblings of children with ASD seem to have no generalized joint attention deficits at 12 and 18 months of age, while siblings with a later ASD diagnosis do show problems with both IJA and RJA. Social-communicative and language problems of the siblings, as measured with the ADOS, M-CHAT and NCDI, were predicted by earlier RJA and developmental index. These predictive variables are thus important for follow-up of infants at risk for ASD.

160.042 42 Autism Spectrum Disorders: Clinical Features in a Large Portuguese Population Sample. F. Duque*¹, S. Mouga², J. Almeida³, C. Café³ and G. Oliveira¹, (1)*Unidade de Neurodesenvolvimento e Autismo – Centro de Desenvolvimento Luís Borges (CDLB), Hospital Pediátrico Carmona da Mota (HP) – Centro Hospitalar e Universitário de Coimbra (CHUC)*, (2)*Faculdade de Medicina da Universidade de Coimbra*, (3)*Hospital Pediátrico Carmona da Mota (HP) – Centro Hospitalar e Universitário de Coimbra (CHUC)*

Background: Autism spectrum disorders (ASD) are a complex, life-long neurodevelopmental disorders characterized by impaired social interaction and communication and by restricted interests and repetitive behaviours. The term high-functioning autism (HFA) is used to refer, among ASD, the individuals without Intellectual Disability (ID). The relevance of Intelligence Quotient (IQ) or Developmental Quotient (DQ) to the symptomatic expression of autism remains unclear. Macrocephaly and parents' education level are clinical features that have been reported since Kanner's original paper. Traditionally, family status variables such as parents' level of education have been regarded as predictors of children's academic achievement.

Objectives: Our aim was to study a large Portuguese population sample of children and adolescents diagnosed with ASD and characterize clinical features between two groups: high-functioning autism (HFA) versus autism with

Intellectual Disability (ID) or global developmental delay (GDD).

Methods: Through computerized data analysis from our Autism Unit, 1188 individuals (979M/209F:4.7/1), who fulfilled the autism diagnostic criteria (all participants had ADI-R and ADOS positive results and DSM-IV-TR criteria), have been included. These sample were divided in two clinical groups, taking into account the classification of ID/GDD of the CID-9 (ID/GDD is present when the IQ/DQ<70), and matched by Full-Scale IQ/DQ score. 290 were HFA (IQ/DQ≥70). We proceeded to statistical analysis of: gender, age of diagnosis, ADIR and ADOS parameters, gestational age, neurodevelopmental profile, head circumference (measured at birth and at time of evaluation) and parents' education level stratified. Statistical analysis (SPSS 19) was performed comparing variables between the two clinical groups. Significance level(σ)=0.05.

Results: The analyzed data showed significant statistical differences between the two groups. Exception to this was in gestational age (pMann-Whitney=0.472). Also head circumference showed similar results in both groups and above those expected from the overall population (~16% vs 3%). At time of evaluation (N=918), 15% of HFA group and 16.8% in the group of autism with ID/GDD had macrocephaly, not observed at birth (N=843), 2.4% and 3.6%, respectively. Parent's education level had similar pattern, however was significantly higher in HFA group ($\chi^2=37.634$; $p<0.001$).

Conclusions: There are differences between high-functioning autism and autism with Intellectual Disability related to diagnostic and anthropometric characterization, personal history and family background. Consistent with prior evidence, macrocephaly occurred at a significantly higher frequency than in the normal reference population. It was also concluded that macrocephaly is not directly related with the severity of autistic symptoms, language or cognitive deficits. As for the parents' education level there is an inverse relationship between it and the severity of autism. What is the implication of these findings for understanding the influence of genetic and environmental factors? In future they should be correlated with genetic analyses. These results have clinical implications, being a

large sample and enhancing the importance of early diagnosis and intervention.

160.043 43 Behavioral Subtypes and Challenging Behaviors. J. Dempsey*¹, S. M. Kanne², S. L. Bishop³ and R. P. Goin-Kochel², (1)*Baylor College of Medicine/Texas Children's Hospital*, (2)*Baylor College of Medicine*, (3)*Weill Cornell Medical College*

Background: Children diagnosed with an autism spectrum disorder (ASD) often exhibit challenging behaviors. Engagement in these behaviors has a high economic and emotional cost for families and communities. Unfortunately, the vast symptom heterogeneity among children with ASD confounds attempts to create targeted treatments for the reduction of these behaviors. Many studies have previously attempted to reduce this heterogeneity through the creation of more behaviorally homogenous subgroups of ASD (Beglinger & Smith, 2001). Few, however, included information from the Autism Diagnostic Interview-Revised (ADI-R), or limited their analyses solely to the core symptoms of autism (i.e., measures of problem behavior, adaptive behavior, IQ, and developmental history were generally included). Fewer still divided repetitive behaviors and restricted interests (RRBs)—considered one of the best predictors of challenging behaviors (Kanne & Mazurek, 2011)—into the repetitive sensorimotor (RSM) and insistence on sameness (IS) sub-categories identified by Richler, Bishop, Klinke, and Lord (2007). Finally, none of the studies attempted to relate the resulting subtypes back to an outcome measure of challenging behavior.

Objectives: (a) To reduce heterogeneity among children with autism through the creation of more homogenous subgroups within the broad population based on patterns of engagement in the core symptoms of ASD as measured by the ADI-R with RRBs separated into the RSM and IS categories; (b) To determine whether the resulting subgroups display differential engagement in challenging behaviors.

Methods: Data was analyzed for children with ASD (probands; $N = 1778$; M age = 6.8 years, $SD = 1.7$ years, range = 4–10 years) who participated in the Simons Simplex Collection (SSC). The RRB domain of the (ADI-R) was divided into RSM and IS scales. These scales along with the current behavior algorithm score in the area of reciprocal social interaction -- labeled

the Social Abnormalities (SA) scale for brevity -- on the ADI-R were entered into a cluster analysis.

Results: The cluster analysis indicated a five-cluster solution. Two clusters, labeled Low Impairment and High Impairment, had low and high scores, respectively, on all three of the scales included in the analysis. The other three clusters, labeled Social Abnormalities, Insistence on Sameness, and Repetitive Sensorimotor + Social Abnormalities, all displayed elevated scores on the scales for which they were labeled. These clusters varied in a systematic and consistent way in their associations with core and associated features of ASD. Notably, the two clusters with relatively high scores on the IS scale (Insistence on Sameness and High Impairment) displayed high levels of emotional and behavioral problems relative to the other groups, but showed no differences from one another on multiple measures of problem behaviors. Surprisingly, these two groups significantly differed from each other on every other variable used in the study (e.g., IQ, communication skills, and adaptive behaviors).

Conclusions: Presently, many treatment packages for challenging behaviors among children with ASD focus on the promotion of communication and social skills. The results of the present study suggest that deficits in these areas or in overall intellectual functioning have little impact on engagement in challenging behaviors in comparison to IS behaviors.

160.044 44 The Link Between Dyadic Synchrony and Maternal Well-Being in Infants At Varying Degrees of Risk for Autism Spectrum Disorders. B. C. Gamber* and A. R. Neal-Beevers, *University of Texas at Austin*

Background: Researchers have demonstrated how maternal internalizing symptoms can have negative consequences on caregiving. However, there is often a transactional relationship between infant development and the caregiving environment (Sameroff, 1975). Thus it is important to consider both sides of the transaction, including effects that mother-infant interaction may have on caregiver well-being. Siller and Sigman (2002) developed a quantitative definition of dyadic synchrony measuring the proportion of a mother's interactions that are sensitive toward and contingent upon her child's focus of attention. Researchers have yet to

examine possible links between dyadic synchrony and maternal well-being. This question may be particularly relevant to mothers of infants with an older sibling with ASD (SIBS-ASD), since parents of children with ASD report increased parenting stress and depressive symptoms (e.g., Duarte et al., 2005; Sanders & Morgan, 1997). In this study, we hypothesized that mothers of SIBS-ASD would report higher depressive symptoms and parenting stress than mothers of infants with a typically-developing sibling (SIBS-TD). Furthermore, we hypothesized that synchrony would be negatively associated with depression and parenting stress across groups, and that this effect would be strongest for mothers of SIBS-ASD.

Objectives: This study will be the first to examine possible associations between dyadic synchrony and maternal well-being in mother-infant dyads with an older child/sibling with or without ASD.

Methods: Twenty SIBS-TD (11 female), 7 SIBS-ASD (5 female), and their mothers were recruited as part of a larger longitudinal study. Data were collected when infants were approximately 9 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 utterances synchronized with infant's attention and action (MS). Mothers completed self-report measures of depression (Center for Epidemiological Studies Depression Scale) and Parenting Stress (Parenting Stress Index- Short Form).

Results: A one-way ANOVA revealed that mothers of SIBS-ASD were experiencing higher parenting stress, $F(1,23) = 19.66, p < .001$, and more maternal depressive symptoms, $F(1,21) = 9.76, p = .005$, than mothers of SIBS-TD. There were no significant differences between groups for MS. Multiple linear regressions indicated a significant interaction effect between sibling risk group and MS on maternal depression (see Figure 1). A similar trend was observed for parenting stress, though the interaction was not statistically significant.

Conclusions: These preliminary results support previous findings of increased depression and

parenting stress for mothers of children with ASD. Moreover, while there was no main effect for synchrony on depression or parenting stress, there was an interaction effect. Higher mother-infant synchrony predicted lower depression scores, but only for mothers of SIBS-ASD. Thus, the transaction between mothers and presently unaffected infants is an important consideration for well-being in mothers of children with ASD. By May of 2013, we will have collected additional data at 9, 12, 15, and 18 months. This will enable us to examine synchrony over time, its relevance to mothers' well-being, and how this differs for SIBS-ASD versus SIBS-TD.

160.045 45 Adaptive Functioning in Toddlers with and without ASD: A Comparison of Two Widely Used Measures. J. Pandey*¹, S. Kauper¹, S. Paterson² and T. IBIS Network³, (1)*Children's Hospital of Philadelphia*, (2)*University of Pennsylvania*, (3)*University of North Carolina- Chapel Hill*

Background: In addition to core deficits, toddlers with autism spectrum disorders (ASD) experience difficulties with adaptive functioning. Adaptive functioning, therefore, is often a target of intervention. However, the relationship between adaptive functioning deficits, IQ, and autistic symptomatology remains unclear. For instance, a study by Liss and colleagues (2001) divided individuals with ASD into high- and low-functioning groups and found that in the high-functioning group only deficits in adaptive behavior were strongly correlated with autistic symptomatology, but that IQ was strongly predictive of adaptive behavior in the low-functioning group. This study and others utilized the Vineland Adaptive Behavior Scales (Vineland) across various ages. To our knowledge, there has been no study to date comparing the Vineland to the Adaptive Behavior Assessment System (ABAS-II) in toddlers with ASD.

Objectives: The objectives of our study are two-fold. The first is to clarify the relationships outlined above and to compare the new edition of the Vineland to another measure, the ABAS-II. The second is to extend the age-range downward from that reported in previous studies, by comparing these two measures in a group of 3-year olds with and without ASD.

Methods: To date, we have studied 28 toddlers (21 males, 7 females; mean age = 38.64 months, SD = 2.95). All children were recruited as part of

the Infant Brain Imaging Study (IBIS). At the age of 3, diagnostic status is confirmed using clinical judgment, taking into account developmental (Mullen Scales of Early Learning (MSEL) and adaptive functioning (Vineland-II), ADOS, and ADI-R. For the purposes of these preliminary analyses, participants were grouped into ASD (n = 9) versus Non-ASD (n = 19), but participants will be stratified by specific autism diagnosis, as well as by specific developmental delay in our final analyses. Total, standard, and calibrated scores from multiple measures will be used to compare these toddlers.

Results: Not surprisingly, a comparison of means across the MSEL, ABAS, and Vineland revealed that in general the Non-ASD group performed better than the ASD group. Using one-way ANOVA, significant differences were found between groups on certain domains of these three measures, but not all. In our limited sample of toddlers diagnosed with ASD, partial correlations revealed strong positive associations between the Composite scores of both the Vineland-II and the ABAS-II, both with and without controlling for developmental functioning. In contrast, in our small sample of Non-ASD toddlers, these measures were not correlated with one another. We will examine these differences as we continue to accrue participants and future analyses will take into account severity of symptom expression as well as the correlations between measures on our sample of Non-ASD toddlers.

Conclusions: Our preliminary analyses demonstrate that in a small group of children diagnosed with ASD, the Vineland-II and ABAS-II are highly positively correlated. These results suggest that either measure of adaptive functioning will appropriately capture these important daily functions. A detailed understanding of these relationships in toddlers should clarify (a) profiles of adaptive behavior difficulties in ASD; and (b) differences in these two commonly used measures.

160.046 46 Language Regression in ASD: A 30-Year Longitudinal Study Investigating Outcomes in Adulthood. S. Harward*¹, M. Farley¹, J. Viskochil², E. Haygeman¹, D. Bilder¹, W. M. McMahon¹ and A. E. Cook¹, (1)*University of Utah*, (2)*Utah Autism Research Program*

Background: Several studies have compared the outcomes of children with and without language

regression; however, no studies to date provide outcome data investigating the early effect of language regression on adult outcomes.

Objectives: To compare current adult functioning of individuals who were diagnosed with autism during childhood and reported to have language regression to those without reported language regression. Current variables of interest are related to social participation, employment, and independent functioning.

Methods: Thirty-year follow-up data for 191 adults (63%) were collected from a population-based sample of 305 adults with ASD. Data on early childhood language regression were available from childhood records for 118 out of the 191 participants (62%) in the follow-up study. Adult variables of interest for the current study include employment status, independent functioning, and social participation. These variables are combined into social functioning composite scores that range from "Very Poor" to "Very Good".

Results: In terms of social functioning outcomes, 28% of those without a reported regression experienced a "Very Poor" or "Poor" outcome, 19% were rated to have a "Fair" outcome, and 11% had a "Good" or "Very Good" outcome. Participants with language regression received the following outcome measures: 12% experienced a "Very Poor" and "Poor" outcome, 7% experienced a "Fair" outcome, and 6% a "Good" or "Very Good" outcome. Analyses of differences in social functioning composite scores for adults with and without early childhood language regression were not significant ($z = -.13$, $p = 0.8$).

Conclusions: The lack of a significant difference in social functioning composite scores suggests that early language regression does not appear to affect later adult outcomes in comparison to those without language regression. This information is compelling, suggesting that while language regression can be devastating for a child with ASD and their family, they have potential to experience adult outcomes that are similar to those without reported language regression.

160.047 47 Autism Spectrum Disorders and the Gender Mixed Brain. J. Eriksson*¹ and S. Bejerot², (1)*Karolinska Institutet*, (2)*Karolinska institutet*

Background:

The 'extreme male brain theory of autism' describes that people with autism spectrum disorder (ASD) have an extreme male pattern of systemising ability and empathising weakness. Clinical experience is, however, that this extreme of maleness does not extend to sexually dimorphic traits like sexuality, social behaviour and gender identity.

Objectives:

To compare measures of sexuality, gender identity and social behaviour between adults with and without ASD.

Methods:

Gender identity and sexuality parameters were measured as a part of a larger controlled study consisting of 50 adults aged 20-47 with high-functioning ASD and 53 age and gender matched neurotypical controls.

Results:

Both males and females in the ASD group reported a decreased sexual drive as well as weak skills concerning assertiveness, leadership and competitiveness. Females in the ASD group reported a less gender identity and increased sexual attraction toward females, while no difference in gender identity or sexual attraction was found between the male groups.

Conclusions:

Unlike systematising and empathising, other sexually dimorphic traits and behaviours does not show extreme male tendencies in the autistic brain. The decreased masculinity in terms of territorial behaviour and sexual drive in both sexes and the masculinised gender identity in women only, suggest a more complicated and gender defiant pattern in the neurological wiring of the brain than proposed by the extreme male brain theory.

160.048 48 Are ADI-R and ADOS-G Sufficiently Sensitive to Identify Rirbs Necessary to Meet the DSM-V Restricted

Interest and Repetitive Behaviours Criteria?. C. Jacques^{*1}, S. Mineau² and L. Mottron², (1)Université du Québec à Ottawa (UQO), (2)Centre d'excellence en Troubles envahissants du développement de l'Université de Montréal (CETEDUM)

Background: Possible decrease of autism spectrum disorder (ASD) prevalence using DSM V, as compared to DSM-IV-TR, is diversely appreciated (30-40% -Matson, Hattier et al. 2012; Matson, Belva et al. 2012; 7%- Huerta et al. 2012; Mazefsky et al. 2012). A related question is how will DSM-V be operationalized in clinical settings. DSM-IV-TR criteria are most frequently operationalized using the Autism Diagnostic Observation Schedule-Generic (ADOS-G) (Lord et al. 2000) and the Autism Diagnostic Interview-Revised (ADI-R). Considering that the DSM-V will now require at least two different elements in the RIRBs domain rather than one like in the DSM-IV-TR ([Http://DSM 5.org](http://DSM5.org)), it seems that the ADI-R and ADOS-G algorithm will retain autistic people with an insufficient number of RIRBs criteria to satisfy DSM-V criteria.

Objectives:

1- To evaluate the nature of RIRBs mostly identified by the ADI-R and the ADOS-G.

2- To evaluate the capacity of ADI-R and ADOS-G to detect the amount of RIRBs necessary to satisfy DSM-V ASD diagnosis.

Methods: The first step consisted in mapping separately RIRBs items of the ADI-R and the ADOS-G domains to the 4 symptoms of the DSM-V RIRBs area. This mapping was then applied to the ADI-R and ADOS-G scoring sheets of a sample of 70 children (age 15-72 months, X =44 mois) randomly selected from the Hôpital Rivière des Prairies database and scoring over the ADOS-G and the ADI-R cut-off for autism. This allowed specifying qualitatively what are the RIRBs symptoms most frequently picked up by the two standardized instruments, and to determine if the autistic children above the third area algorithm in each of the two instruments were or not positive to the cut-off for this area in the DSM-V.

Results: The RIRBs symptoms mostly detected by the ADI-R were repetitive use of objects (mean frequency= 1,1), followed by unusual sensory interests and unusual preoccupations (0,9), and

mannerisms (0,8). The RIRBs mostly observed in the ADOS-G were excessive interest (1,5), followed by unusual sensory interest in play (1,3), and mannerisms (0,9). 8 (11,4%) children positive on ADI-R third area algorithm and 17 (24,3%) children positive on ADOS-G third area algorithm do not meet RIRBs cut off in the DSM-V criteria. The intersection of the children undetected by the combination of the two standardized instruments resulted in 5 (7,1%) subjects positive for the DSM-IV-TR criteria of the RIRBs domain, but which did not reach the DSM-V cut off in the RIRBs domain.

Conclusions: These preliminary finding suggest that some autistic children diagnosed on the basis of the DSM-IV-TR will not meet the criteria of RIRBs domain of the DSM V. The next step of the present study will be to evaluate the frequency and the nature of RIRBs in a larger sample including wider age range and milder phenotypes and analyse the RIRBs separately according to the module of the ADOS and ADOS-2 (1, 2 and 3).

160.049 49 The Social Responsiveness Scale: The Relation to Parent Rated Social Outcomes in Youth with ASD. K. Johnston* and G. Iarocci, *Simon Fraser University*

Background: The Social Responsiveness Scale (SRS; Constantino, 2005) is a parent/teacher-report measure of social impairment associated with Autism Spectrum Disorders (ASDs) and is widely used as a screening tool and as an aid in clinical diagnosis. In contrast to tests such as the Autism Diagnostic Interview-Revised (ADI-R; Le Couteur et al., 1989), which is designed to classify an individual as either having ASD or not, the SRS is intended to assess the full spectrum of symptom severity in the general population. Although empirical evidence has found that the SRS has demonstrated strong convergent validity (e.g., Constantino et al., 2003), it is also important to determine whether SRS scores (as an index of social impairment) also possess criterion-related validity; for example, relate to reports of actual social outcomes among youth with ASD.

Objectives: This study examined the relationship between SRS scores and parent reports of real-world social outcomes such as peer relations in a sample of high functioning youth with ASD. It was hypothesized that higher scores on the SRS (indicating higher social impairment) would be

associated with poorer peer relations in this sample.

Methods: Data from 51 youth with high functioning autism (i.e., IQ >85) between the ages of 7 and 18 was utilized. All relevant data was 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. SRS raw score data was correlated with data from a brief parent questionnaire inquiring about the quality of their child's peer relationships. Items on this questionnaire ask parents to rate how well certain statements, such as "gets along with his/her classmates" or "is ignored by peers at school", describe their child on a 4 point scale (never, rarely, sometimes, often, or almost always).

Results: Results showed that SRS raw scores were significantly negatively correlated with parent-reports of social outcomes ($r=-.526$, $p<.001$) among high functioning children with ASD. Using Cohen's (1992) criteria, this qualifies as a large effect size.

Conclusions: Our prediction that higher scores on the SRS (indicating higher social impairment) would be related to poorer peer relations in a high functioning sample of youth with ASD was confirmed. These findings contribute further support for the SRS as a valid measure of social impairment among high functioning youth with ASD.

160.050 50 Reward Learning Influences Social Reciprocity: The Impact of Autistic and Behavioural Inhibition Traits. M. S. Panasiti*, I. Puzzo and B. Chakrabarti, *University of Reading*

Background: Autism Spectrum Conditions are characterized by social deficits that often co-occur with symptoms of behavioural inhibition and social anxiety (White et al, 2009). Behavioural interventions based on reward learning (e.g. ABA therapy) have been found to be effective on improving these deficits (Zachor et al, 2007). However, the efficacy of such interventions shows considerable inter-individual variability (Howlin et al, 2009) and is lower for social avoidant individuals (Ingersoll et al, 2001). It is not clear whether autistic or behavioural inhibition traits modulate the sensitivity to a) reward learning or

b) the ability to translate the learned associations to social behaviours.

Objectives: In this study we tested: a) if autistic or behavioural inhibition traits could modulate the ability to implicitly associate a reward value to a social stimulus (reward learning/conditioning); b) if the learned association could modulate participants' social behavior (i.e. social reciprocity); c) if the strength of this modulation was mediated by traits of autism or behavioural inhibition.

Methods: 18 neurotypical adults (8 Males) were administered with an evaluative conditioning paradigm used to associate high or low reward values with neutral target faces. Subsequently, participants performed a ball-tossing game with the high-reward (PosFace) and low-reward (NegFace) faces. PosFace and NegFace reciprocated participant's ball-tossing with the same probability (50%). To test the impact of reward conditioning on social reciprocity, we divided the number of tosses directed to the PosFace by the number of tosses directed to the NegFace. Subsequently we used the Implicit Association Task (IAT) to assess the strength of conditioning (i.e. the strength of the association between PosFace and win-pictures and NegFace and loss-pictures). All participants completed the Autism Spectrum Quotient (AQ) and Behavioural Inhibition System (BIS) questionnaires online.

Results: 1) Overall, we found an effect of conditioning on IAT scores. Incongruent blocks (PosFaces paired with loss-items; NegFace paired with win-items) required longer reaction times than congruent blocks (PosFace paired with win-items; NegFace paired with lose-items). This suggests that there was a significant effect of reward learning. This effect was not correlated to AQ or BIS.

2) We found that the number of ball tosses to the PosFace compared to the NegFace in the ball-tossing game was positively correlated with strength of conditioning ($r=.524$) and negatively correlated with the BIS scores ($r=-.714$). This suggests that reward learning has an effect on the extent of social reciprocity. No effect of AQ was found.

3) BIS scores were found to moderate the effect of conditioning on social reciprocity ($\beta=2.4$). This suggests that more inhibited the participants were, the less did the learned reward value of the face have an impact on social reciprocity.

Conclusions: Our data show that neither AQ nor behavioural inhibition traits impact the ability to associate a reward value to a social stimulus. Nevertheless, high inhibition traits seem to impair the ability to translate this reward value to social reciprocity. This has potential implications for autism therapy, in that behavioural therapies relying on conditioning techniques may be less effective for autistic individuals who show high behavioural inhibition.

Psychiatric/Behavioral Comorbidities Program

161 Mental Health

161.051 51 Persistent Intolerance of Uncertainty: A Mechanism for Anxiety in Children with ASD?. M. South*¹, S. White², P. D. Chamberlain¹, M. H. Freeston³ and J. Rodgers³, (1)*Brigham Young University*, (2)*University of California, Davis*, (3)*Newcastle University*

Background: The inability to tolerate uncertainty is associated with some aspects of anxiety (Birrell, 2008). Intolerance of uncertainty (IUC) in environment or routine may underlie high levels of co-morbid anxiety seen in autism spectrum disorders, including associations between anxiety and repetitive behavior (ASD; Rodgers et al., 2012). To our knowledge, however, there are no known experimental manipulations of IUC in ASD samples.

Objectives: We explored how psychophysiological response would differ according to various combinations of uncertainty and threat (certain safety, certain threat, and uncertain threat) in ASD and matched control (CON) groups. We hypothesized that uncertainty would be particularly aversive for the ASD group and that measures of IUC would predict this response.

Methods: Here we report data for two experiments: the first with a group of children ages 8-11 (26 ASD, 31 CON) and the second with older teens (ages 15-18; 25 ASD and 25 CON). For the younger group, the top card on a computerized deck revealed either a feather that would spare a virtual balloon after a 30-second timer, a pushpin that would pop it, or a question

mark that left the outcome in doubt until the timer was finished. We measured skin conductance response (SCR) during each 30-second block and also during a 30-second recovery period of watching a soothing underwater scene. The older teens were shown varied computer contexts where they knew that a startling airpuff to the neck would not occur, occur during a particular cue, or occur in that context but independent of the cue. The dependent measure was EMG eyeblink response to white-noise startle probes occurring during each condition

Results: Experiment 1 with the children showed similar SCR response in each group during the threat phase, but critically a failure in the ASD group to calm during the recovery period following the uncertain condition. In the ASD group, SCR response to the task was specifically associated with the parent-reported Intolerance of Uncertainty Scale, and not with more general anxiety scales. There were similar strong positive associations with SCR response, IUC scores, and autism symptom severity from the Social Responsiveness Scale. No such associations were seen in the CON group. In Experiment 2 the ASD group failed to habituate as quickly over the course of the task and response in contexts following an uncertain context was exaggerated relative to controls.

Conclusions: These data suggest that while both ASD and CON samples are bothered by uncertainty, the ASD group has specific difficulty in calming down after such situations. This inability to recover from uncertainty may represent one mechanism for anxiety and resistance to change in ASD. We are building a model that considers both cognitive and physiological inputs to anxiety in ASD that may have a different balance in ASD versus anxiety in children without autism symptoms. These studies demonstrate the potential value for designing explicit experimental tests of IUC that can be manipulated to explore, for example, the relative response to reward versus threat or variations in timing of arousal and recovery.

161.052 52 A New Perspective: A Network Analysis of Repetitive Behaviors in Autism and Obsessive Compulsive Disorder. L. M. Ruzzano*, D. Borsboom and H. M. Geurts, *University of Amsterdam*

Background: Associations between restricted and repetitive behaviors (RRBs) in autism and OCD have been of particular interest, due to elevated rates of comorbidity, as well as neurological and behavioral findings implying symptom overlap. Compulsions in OCD are maladaptive strategies used to cope with the perceived distress of the obsessions (Markarian et al., 2010). However, the functional relationship between obsessions and compulsions lack valid evidence among individuals with autism due to difficulties in describing their mental states and experiences. Rather, it has been suggested that RRBs in autism may be a function of efforts to manage unusual sensory processing (Baker et al., 2008). Thus, the debate regarding symptom overlap is dependent on the interaction between RRBs. Yet, to date, standard methods have been limited in their ability to accurately reflect the interrelations of RRBs in autism and OCD.

Objectives: To investigate the role of and interrelations between RRBs characteristic of autism and OCD through the use of Network Analysis. Specific aims were to: (1) assess whether autism and OCD represent distinct disorders (e.g., separate symptom clusters); (2) compare the frequency of causal symptom relations in autism and OCD; (3) and assess the importance of (e.g., centrality) of compulsions in the network.

Methods: Network analysis was used to assess relations between RRBs in autism and OCD. In the network perspective, symptoms exist as a dynamic interacting system, where a disorder is a cluster of highly correlated symptoms (Cramer, Waldorp, van der Maas, & Borsboom, 2010). Thus, what binds a set of symptoms is a dense set of direct causal relations between symptoms. This study constructed network models based on two samples. First, a network was constructed based on seven clinicians who were asked to rate causal association between RRBs characteristic of autism and OCD. Second, a network model was constructed based on a clinical sample of 213 children. The two networks were visually assessed and compared according to the three objectives previously stated. Characteristics of specific symptoms were analyzed by computing various centrality measures.

Results: Symptoms clustered in correspondence with autism and OCD. Within each disorder, symptom connections were stronger and more frequent. Compulsions were most central across both networks. However, autism symptoms were found to be more strongly connected and cause more symptoms than OCD symptoms in the clinical sample network. In addition, sensory symptoms and verbal rituals showed high centrality estimates in the network.

Conclusions: Autism and OCD are characterized by significantly different patterns of interaction between RRBs. Compulsive symptoms served as a main link between autism and OCD. Sensory symptoms and verbal rituals were found to be valuable in our understanding of RRB interactions. In addition, our results support proposed changes to the DSM-5 to include sensory symptoms and verbal rituals to the RRB domain of autism. While further research is needed, this study demonstrates the importance of symptom interrelations in understanding the association between autism and OCD.

161.053 53 ASD Characteristics in Elderly with Mood and Anxiety Disorders. H. M. Geurts*¹ and H. Comijs², (1)*University of Amsterdam*, (2)*GGZInGeest / Vu University Medical Center*

Background:

Recently it was shown that the prevalence of autism spectrum disorders (ASDs) is 1% independent of age. However, in elderly it could well be that ASD is not yet recognized as such as when these elderly were children, specific ASD diagnoses were not broadly known. Moreover, it has been acknowledged relatively recently that ASD can be present among all possible intelligence levels. The most common earlier diagnoses for adults with ASDs who received their ASD diagnosis in adulthood were mood and anxiety disorders (Geurts & Jansen, 2011). Hence, we hypothesize that especially in elderly known with mood and anxiety disorders there will be undiagnosed cases of ASD.

Objectives:

We investigated whether in elderly with a history of mood and anxiety disorders a larger number of these elderly would score above the clinical cut off

of an autism screening instrument than elderly without such a psychiatric history.

Methods:

The short version of the Autism Spectrum Quotient (short AQ; 28 items; self report; Hoekstra et al., 2010) was filled out by 117 healthy elderly (Controls; M=69 years, 44 males/73 females) and 259 elderly with a known history of mood and anxiety disorders (Mood; M=70 years, 83 males/167 females). A cutoff of 70 (4-point scale) was used. None of the included elderly was known with an ASD diagnosis, and all elderly took part in a large longitudinal cohort study (NESDO).

Results: In the healthy elderly group 5.1 % had a score above the short AQ cutoff, while in the mood disordered group 30.9% scored above this cutoff. There was a significant correlation of age and AQ for the controls ($r=.30$), but not for those with a known history of mood disorders ($r=-.10$). In both groups we observed significant correlations of the AQ score with anxiety (Controls $r=.41$;Mood $r=.30$) and mood self-reports (Controls $r=.37$; Mood $r=.32$).

Conclusions: As predicted, a larger proportion of elderly with a history of mood disorders showed more ASD characteristics. Moreover, an increase in the severity of the ASD characteristics was related to an increase in self-reported anxiety and mood problems. However, this does not necessarily implies that there is indeed a larger number of missed ASD cases in this sample of elderly with mood disorders, but does warrant a follow up study to determine whether the AQ can be used in such a specific group of elderly to detect previously missed cases of ASD.

161.054 54 Affective Symptoms in Adolescents with Autism:

Differentiating the Correlates of Anxiety, Depression and Irritability. E. Simonoff*¹, T. Charman², F. Happé³, G. Baird⁴, C. Jones⁵ and A. Pickles⁶, (1)*Institute of Psychiatry, King's College London*, (2)*Institute of Education*, (3)*SGDP, IoP, King's College London*, (4)*Guy's Hospital*, (5)*University of Essex*, (6)*University of Manchester*

Background: People with autism are known to be at increased risk for a range of mental health problems and also have increased rates of 'challenging behaviour,' in which there is severe

defiance and aggression towards self and others. However, the relationship between these two elements is poorly understood and, in particular, the affective components that may play a role in challenging behaviour in autism are not well-characterized.

Objectives: To explore the role of different mental health problems, most especially affective symptoms, in severe behavioural disturbance or challenging behaviour in autism; To explore whether there is an additional and specific role for neurocognitive characteristics often seen in autism (such as emotion recognition, theory of mind) in influencing challenging behaviour.

Methods: This study uses data from the Special Needs and Autism Project (SNAP), a longitudinal, population-based cohort of 100 adolescents with ASD assessed at both 12 and 16 years. A measure of *severe mood problems (SMP)* was previously developed from the Profile of Neuropsychiatric Symptoms (PONS) and included: low mood, depressive thoughts, labile mood and explosive rage. Symptoms of anxiety, irritability and oppositionality were further added as potential contributors to challenging behaviour. Autism severity was measured with the Social Responsiveness Scale (SRS) and autism diagnostic classification was childhood autism/any other PDD. IQ was measured on the Wechsler Abbreviated Scale of Intelligence. Theory of mind was assessed with the animated triangles, emotion recognition with the Ekman faces, and flexibility with the Card Sort and Trails tests.

Results: Data were available on 91 participants, of whom the top quartile was a priori described as having SMP. As previously reported, SMP was associated with more generalized mood problems and conduct problems (both $p<.001$), but when temper tantrums symptom of conduct problems was accounted for, the association with conduct problems fell to .055, suggesting a more specific link to irritability. Intellectual ability and autism severity were not associated with SMP, however both were linked to elements of conduct problems, suggesting a more specific relationship. Associations between SMP and tasks of emotion recognition and flexibility were not significant once intellectual ability was accounted for. For this presentation, further analyses will be undertaken to include symptoms of anxiety and

irritability/temper/oppositionality to parse the independent and shared effects on mood problems and to identify the clusters of problems that exist in adolescents with autism and their neurocognitive correlates.

Conclusions: Findings with respect to severe mood problems in adolescents with ASD suggest that the neurocognitive underpinnings of these difficulties are different from those reported in adolescents that are otherwise typically developing. A broader exploration of the psychiatric and neurocognitive correlates of severe mood problems and challenging behaviour is needed to develop effective interventions.

161.055 55 Aggressive Behaviors in ASD: Prevalence and Correlates in a Large Clinical Sample. A. D. Hagen*¹, D. J. Kriz¹, S. W. Duvall¹, D. Ettinger¹, C. Green¹, A. P. Hill¹, K. Freeman¹, J. van Santen¹, J. Nigg¹, D. A. Fair¹ and E. Fombonne²,
(1)*Oregon Health & Science University*, (2)*Oregon Health and Sciences University*

Background: Aggressive behaviors are frequent in Autism Spectrum Disorders (Kanne and Mazurek 2010; Matson and Rivet 2008) and associated with more intensive medical interventions, impairment, and increased demands on caregivers (Lecavalier and Wiltz 2006). Despite the high importance of this subject, it is not well studied.

Objectives: To investigate the prevalence of aggressive behaviors in ASD children at the time of diagnosis, and to identify age and gender trends and other factors that are associated with them.

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. Aggressive behaviors were measured on the Aggressive behavior scale of the CBCL that provided as well measurements of co-occurring emotional and behavioral problems. Data on parental concerns, autism severity, adaptive behavior, verbal level, medication use, socio-demographic background were available through parental self-reports and standardized professional questionnaires recorded in the ATN database.

Results: Aggressive behaviors were one of the most frequent (55.6%) parental concerns at referral. 25% of children were scoring in the clinical range for aggressive behaviors as measured by a T-score above 70 on the Aggressive scale of the CBCL. Aggressive behaviors were unrelated to age ($p=.25$), gender ($p=.22$), parental education ($p=.29$), to non verbal status ($p=.29$), clinical evidence of cognitive delay ($p=.32$), autism severity as measured by DSM-IV symptom count ($p=.70$) and to Vineland standard scores. Aggressive behaviors were strongly related with T-scores falling in the clinical range in all other subscales of the CBCL. Correlations with other factor and total CBCL scores ranged between .33 (Somatic complaints) and .95 (Externalizing score) (all $p<.001$). Aggressive behaviors significantly increased the likelihood of psychotropic drug prescriptions (43% vs 29%; $p=.01$) but not that of alternative medicines (33.3% vs 27.3%; NS). We performed further analyses by comparing 88 children scoring above a t-score of 70 on the CBCL aggressive subscale (Agg+) to 183 children scoring under 60 on the same scale (Agg-). Bivariate logistic analyses were performed to identify predictors of Agg+. Results showed the same pattern than in the whole sample with gender, age, Vineland scores, verbal level, and sociodemographic variables bearing no association with presence/absence of aggressive behaviors. Association with multiple comorbid syndromes were significant, with a particularly strong association with ADHD symptoms. More detailed analyses will be presented alongside results of multivariate logistic regression models.

Conclusions: Aggressive behaviors are a significant source of parental concern and have consequences in the management (medication or otherwise) of ASD children. Correlates of aggressive behaviors in typical children were weaker or absent in this ASD sample, possibly pointing to a different mechanism and significance of aggression in ASD. Similarly, aggressive behaviors were not predicted by indices of autism severity. High levels of both internalizing and externalizing co-occurring symptoms, especially with ADHD symptoms, are cues for further studies.

161.056 56 Anxiety Disorders in Autism Spectrum Disorders (ASD) without Intellectual Disabilities. M. Soussana, J. Brisot-

Background:

People with ASD have specific impairments in socio-communicative skills, including facial emotional expression recognition (WHO, 1993). Previous studies reported a high prevalence of anxiety in Autism Spectrum Disorders (ASD) without intellectual disability (White, Oswald, Ollendick, et al. 2009). We hypothesized that the deficits in facial emotion recognition would be associated with anxiety disorders in this population.

Objectives:

The purpose of this study was 1) to explore the relationship between anxiety disorders and facial emotional expression recognition in adolescents with ASD without intellectual disability and in a control group of adolescents without ASD, and 2) to characterize anxiety disorders in ASD without intellectual disability.

Methods: Our study is cross-sectional, descriptive and comparative. Forty-six adolescents with ASD without intellectual disability aged between 11 and 18 years participated in the study. Among them, 20 had an anxiety disorder and were compared with 20 controls of the same age, with anxiety disorder without ASD. Anxiety disorder was assessed with a parent and adolescent interviews: the Schedule for Affective Disorders and Schizophrenia for School-Age Children, Present and Lifetime Version (K-SADS-PL, Kaufman et al., 1997) according to DSM-IV criteria. Facial emotional expression recognition was studied using the DANVA 2F test (Nowicki & Carton, 1993), that consist of 24 photographs of male and female facial expressions of *Happy*, *Sad*, *Angry* and *Fearful* emotions.

Results:

In adolescents with ASD, anxiety disorders were related to impairments in recognition of the emotions *Anger* and *Sadness*. Moreover, we found a significant correlation between the level of social anxiety and improvement in *Fear* recognition that was specific to ASD.

Conclusions:

This study support the hypothesis that anxiety disorders are related to facial emotion recognition in adolescents with ASD without intellectual disability. Clinical implications concerning the assessment of anxiety comorbidities in this population and the lack of adapted treatments are discussed.

161.057 57 Attentional Biases to Emotional Faces in People with Autism Spectrum Disorders & Co-Occurring Anxiety. A. Ozsivadjian*¹, M. J. Hollocks², P. Howlin² and E. Simonoff², (1)*Guy's Hospital*, (2)*Institute of Psychiatry, King's College London*

Background:

People with ASD are known to display increased levels of anxiety symptoms and disorders. To date, there has been little research examining the cognitive mechanisms of anxiety in ASD. One area of interest is to know whether children with ASD and anxiety show similar attentional biases to threat compared to non-ASD children with anxiety disorder.

Objectives:

To examine whether children with an ASD display anxiety related attentional biases towards threatening faces and to investigate possible relationships between biases, anxiety and affect recognition.

Methods:

This study is ongoing and currently includes 38 boys with ASD recruited from specialist schools and 41 typically developing controls. At the time of presentation an additional clinically selected group of ~50 children with ASD will also be presented. All participants were aged between 10 and 16 years and had a full-scale IQ ≥ 70 . Anxiety was assessed using the Spence Child Anxiety Scale (SCAS) – parent version.

Attentional bias was examined using the visual-probe task commonly used in the child anxiety literature. Participants were presented with angry or happy faces paired with neutral faces followed by an emotion-congruent or incongruent probe. Bias scores were calculated by deducting the

mean RT for congruent trials from the mean RT for incongruent trials. Affect recognition was also assessed to control for known deficits in emotional face processing in ASD using the affect recognition sub-test of the NEPSY-II test battery.

Results:

The groups significantly differed on age (ASD mean 12 years vs. controls 14 years, $p \leq .05$), full scale IQ (96 vs. 113, $p \leq .01$) and the ASD group had significantly higher anxiety ratings (SCAS-P; 29 vs. 8, $p \leq .01$).

Attentional bias - A multivariate regression analyses examined the relationship between group, anxiety and the bias scores from both threat & happy faces. When taking into account both FSIQ and anxiety no significant group differences were found for either angry ($\beta = 3.6$, $p = .81$) or happy faces ($\beta = 6.9$, $p = .45$).

Affect recognition - Children with ASD performed significantly worse on the standardized test of affect recognition (7.9 vs. 10.2, $p \leq .01$). However, affect recognition score was not significantly related to either angry or happy face bias, in the whole sample, or in the ASD and control groups individually. Affect recognition was inversely related to SCAS scores in whole sample ($\beta = -3.3$, $p = .012$), but not in the ASD and control groups individually.

Conclusions:

While children with ASD displayed elevated levels of anxiety the expected bias towards threat was not observed. In addition ability to recognise emotional faces was not related to either bias score or levels of anxiety in the ASD group. Our results may suggest that despite showing elevated levels of anxiety, those with ASD may not display the same cognitive correlates of anxiety seen in non-ASD children. This may suggest that the underlying cognitive mechanisms of anxiety in ASD are distinct from their typically developing peers. Additional data, study limitations and alternative hypotheses will be discussed.

161.058 58 Autism Spectrum Disorders in Children and Adolescents with Attention Deficit Hyperactivity Disorder. S. Herguner* and A. Herguner, *NE University, Meram Faculty of Medicine*

Background: Attention deficit hyperactivity disorder (ADHD) is characterized by severe inattention, hyperactivity, and impulsivity. Autism spectrum disorders (ASD) are characterized by impairments in social interaction and communication as well as repetitive and restricted behavior and interests. Current classification systems (ICD-10, DSM-IV) do not allow for a comorbid diagnosis of ASD and ADHD and there is a hierarchy of diagnosis, whereby a diagnosis of ASD overturns that of ADHD. Despite the diagnostic rules, many research studies have documented coexistence of ASD and ADHD diagnoses. ADHD and ASD appear to often co-occur in families. Several studies reported that 30–80% of children with ASD meet criteria for ADHD and 20–50% of children with ADHD meet criteria for ASD.

Objectives: We aim to investigate the frequency of autism spectrum disorders in clinic-referred children with ADHD and compare psychiatric comorbidity between children with ASD plus ADHD and only ADHD.

Methods: A consecutive series of 147 children and adolescents (mean age, 9.95 ± 3.02 y) with a diagnosis of ADHD were included in the study. All cases were interviewed by the first author for autism spectrum disorders according to DSM-IV criteria. Psychiatric co-morbidity was assessed using the Schedule for Affective Disorders and Schizophrenia for School Age Children-Present and Lifetime Version (K-SADS-PL-T).

Results: Fourteen cases (9.5 %) were diagnosed as having a comorbid ASD (3 with autistic disorder, 3 with Asperger syndrome and 8 with PDD-NOS). Subjects with ASD plus ADHD were compared with subjects with ADHD without ASD. Hyperactive-impulsive subtype was more frequent in ADHD plus ASD group. ADHD and ASD comorbidity was significantly associated with a higher rate of males. Frequency of psychiatric disorders was higher in ADHD and ASD group.

Conclusions: Family and twin studies supported the hypothesis that ADHD and ASD originate from partly similar genetic factors. A screening for ASD

should be performed in patients with ADHD, as these patients and their parents are frequently not aware that the impairment may be partly due to a comorbid ASD.

161.059 59 Autistic Traits Predict High Self-Perceived Stress and Poor Coping in High-Functioning Adults with ASD. T. Hirvikoski* and M. Blomqvist, *Karolinska Institutet*

Background:

Despite normal intellectual capacity, autistic traits may complicate performance in many everyday situations. Thus, common everyday situations that require social interaction, communication and/or behavioural flexibility may constitute stressors for high-functioning individuals with ASD. Internal or external stimuli that an individual perceives as threatening (i.e. stressors) disturb the dynamic equilibrium of the body (i.e. homeostasis) and elicit a stress reaction. It is not only the individual's perception of threat/stressors that is crucial for the perception of distress, but also the individual's subjective perception of his or her ability to cope with the specific stressor, or perception of control.

Objectives:

The aim of the study was to describe level of subjective stress in everyday life and self-perceived ability to cope with stress in adults with high-functioning autism spectrum disorders (ASD), adults with attention-deficit/hyperactivity disorder (ADHD; i.e. another clinical group known to report high subjective stress), and controls from general population. Second aim was to study association between autistic traits and self-perceived stress and coping.

Methods:

Seventy-four adults (25 with ASD; 21 with ADHD; 28 controls from general population) completed the Perceived Stress Scale. The results in the PSS were analysed using a two-factor solution (PSS Distress versus PSS Coping) based on a previous factor analysis. Autistic traits were assessed using the Autism Spectrum Questionnaire (AQ) that measures a variety of behaviours and characteristics typically observed in individuals with ASD, or "autistic traits". The AQ is not only sensitive in diagnosed individuals but can also

detect variance in non-clinical autistic traits. The AQ was completed by individuals with ASD and controls.

Results: The three groups (ASD, ADHD, and controls from general population) were comparable with regard to age, within-group gender distribution, Swedish versus non-Swedish origin, as well as educational level. However, the controls more often worked or studied fulltime as compared to the groups with neurodevelopmental disorder. Both adults with ASD and ADHD reported significantly higher subjective stress and poorer ability to cope with stress in everyday life, as compared to controls (large effect sizes), while the clinical groups did not differ from each other. Autistic traits (total score of AQ) correlated with PSS Distress ($r = .64, r^2 = .41, p < .001$) and PSS Coping ($r = .63, r^2 = .40, p < .001$). A mediator analysis revealed that also when controlling for the possible mediator role of the Coping subscale, the AQ still significantly predicted the Distress subscale scores (standardized beta coefficient = $.42, p = .002$). Thus, autistic traits were an independent predictor of both subjective stress/distress and coping in this cross-sectional material.

Conclusions:

ASD is associated with high level of subjective stress and perception of poor coping ability in high-functioning individuals. Long-term consequences of chronic stress in everyday life as well as treatment intervention focusing on stress and coping, should be addressed in future research as well as in clinical management of ASD in high-functioning adults.

161.060 60 Autistic Traits in Children with ADHD Index Clinical and Cognitive Problems. J. Martin*, M. Cooper, K. Langley, M. Hamshere and A. Thapar, *Cardiff University*

Background: Traits of autistic spectrum disorders (ASD) occur frequently in attention deficit hyperactivity disorder (ADHD), but the significance of their presence in terms of phenotype and underlying neurobiology is not properly understood.

Objectives: This analysis aimed to determine whether higher levels of autistic traits index a

more severe presentation in a large, rigorously phenotyped sample of children with ADHD.

Methods: A clinical sample of children meeting research diagnostic criteria for ADHD with no known diagnosis of ASD (N=711) was assessed using parental report (interview and questionnaires) and psychological assessment (IQ and reading tests) on measures of autistic traits (via the Social Communication Questionnaire (SCQ)), as well as clinical comorbidities and cognitive and developmental features. Multivariate regression analyses were used to examine association of SCQ scores with core ADHD features and clinical, cognitive and developmental outcomes, with adjustment for putative confounders. For outcomes showing association with total SCQ score, post-hoc analyses explored levels of differential association of the three ASD sub-domains (social deficits, communication deficits and restrictive and repetitive behaviours (RRBs)).

Results: Results suggest that increasing ASD symptomatology within ADHD is associated with a more severe phenotype in terms of oppositional, conduct and anxiety symptoms, lower full-scale IQ, working memory deficits and motor problems. These associations persisted after accounting for ADHD severity, suggesting that autistic symptomatology independently indexes the severity of comorbid impairments in the context of ADHD. ASD sub-domain scores did not show unique contributions to most outcomes. The only exceptions were that social deficits were independently associated with oppositional symptoms and RRBs independently predicted hyperactive-impulsive symptoms and motor problems.

Conclusions: Autistic traits in children with ADHD appear to index higher levels of phenotypic complexity. As such, the results suggest that it is important to consider levels of socio-communicative and repetitive traits in children with ADHD who do not meet diagnostic criteria for ASD, as these may have implications for the efficacy of interventions.

161.061 61 Catatonia in Autism Spectrum Disorders: A Diagnostic, Therapeutic, and Scientific Conundrum. D. M. Dhossche*, *University of Mississippi Medical Center*

Background: Catatonia has been associated with intractable aggression, stereotypy, and self-injury in patients with autism spectrum disorders, and represents a diagnostic, therapeutic, and scientific conundrum in this population

Objectives: To review the literature on diagnosis, treatment, and risk factors of catatonia in autism spectrum disorders.

Methods: Literature review and review of case-reports

Results: Recent studies document catatonia as a comorbid syndrome at a rate of 12-17% in adolescents and young adults with autism spectrum disorders. Lacking controlled trials, benzodiazepines and ECT have been administered safely in case-reports and case-series, sometimes with remarkable and lasting improvements. Barriers to increase this topic's visibility are its novelty in the field of autism spectrum disorders, the lack of independence of catatonia as a separate syndrome in psychiatric classification, and the stigma surrounding the use of benzodiazepines and electroconvulsive therapy, the medical treatments that seem most effective in catatonia

Conclusions: There have been advances during the last ten years in demarcating catatonia as a treatable condition in autism spectrum disorders and as a distinct scientific field of inquiry, yet the condition remains poorly recognized and studied. Further study of catatonia in autism spectrum disorders may provide new diagnostic, therapeutic, and scientific opportunities.

161.062 62 Child, Parent, and Systemic Correlates of Comorbid Anxiety and Depression in Adolescents and Adults with ASD. J. A. Weiss*¹, A. Tint¹ and Y. Lunsky², (1)*York University*, (2)*Centre for Addiction and Mental Health*

Background: Symptoms of anxiety are one of the most common mental health problems in individuals with autism spectrum disorders (ASD), with the majority having some level of impairment attributed to anxiety (White et al., 2009). Although less common, depression is also noted as a major concern (Hedley et al., 2006). Little is known about how individual with ASD who experience comorbid anxiety and depression differ from those with only anxiety or those without any

internalizing problems. Understanding the factors that differ among these groups can help us tailor interventions more effectively.

Objectives: This study examines child (age, gender, ASD symptom severity, intellectual ability, aggression), parent (age, gender, education, service and caregiver efficacy, and burden), and social and systemic factors (family distress, negative life events, history of emergency department and hospital use, current mental health care use) that differentiate people with ASD with a history of anxiety and depression from those with no history of internalizing symptoms and those with only a history of anxiety problems.

Methods: As part of an online survey, 330 parents ($M = 48.9$, $SD = 7.4$) of adolescents and adults with ASD ($M = 18.4$, $SD = 5.8$) completed brief measures of children's problems with depression, anxiety, and aggression (Yes/No), severity of ASD symptoms (Social Communication Questionnaire; Rutter et al., 2003), level of intellectual functioning (parent report), family distress (Brief Family Distress Scale; Weiss & Lunsky, 2011), caregiver mastery and burden (Revised Caregiving Appraisal Scales; Lawton et al., 2000), history of emergency room visits and psychiatric hospitalizations, and negative life events in the last two months. The majority of parents were mothers (94%).

Results: Only 14% of the sample did not have a history of problems with anxiety or depression, compared to 50% with only anxiety and 35% with depression and anxiety. Only 1% were noted to have depression only, and as such were removed from analyses. As expected, individuals with anxiety and anxiety/depression received more mental health services and were more likely to have a problem with aggression than those without internalizing symptoms. Parents of individuals with anxiety/depression reported lower rates of perceived service and caregiving efficacy than parents of individuals with no internalizing symptoms. Individuals with ASD and depression/anxiety had higher intellectual functioning, more negative life events, more family distress and were more likely to have visited the emergency department and have had a psychiatric hospital admission than individuals

with only anxiety and those with no internalizing symptoms (all p 's < .001).

Conclusions: The present findings describe the challenges faced by adolescents and adults with ASD and their parents, when children have comorbid anxiety and depression. Possibilities for intervention and future research will be discussed.

161.063 63 Clinical Correlates of Personality in ASD. J. P. Teunisse*¹, A. van der Sijde² and H. Berger³, (1)*Dr Leo Kannerhuis*, (2)*Yulius Autisme*, (3)*Radboud University Nijmegen Medical Centre*

Background: Addressing the heterogeneity of autism spectrum disorders (ASD's) has challenged clinicians and researchers alike. Identifying subtypes according to language-, behavioral- or cognitive characteristics seems fruitful, however introduces the risk of over-simplifying the condition and loosing 'the individual' out of sight. We propose that especially in the framework of clinical intervention, subtyping autistics according to *personality* may be more useful. Although historical accounts and recent research suggest that people with ASD show specific personality traits, as yet not much is known about the clinical correlates of personality in the ASD population.

Objectives: The current research tries to elucidate whether persons with ASD score differently on the 'big five' personality traits in comparison to the norm population. In succession it will be evaluated whether personality traits or - profiles of persons with ASD are associated with observed variance in the expression of autism symptoms, related cognitive styles and general psychological wellbeing.

Methods: A group of 99 high functioning adolescents and young adults diagnosed with ASD was screened on (1) therapist-rated and self-reported autism symptomatology using respectively the Autisme Beoordelings Lijst (ABL, autism evaluation list) and Autism Spectrum Quotient (AQ), (2) personality using the NEO-Five Factor Inventory (NEO-FFI), (3) cognitive style (several measures targeting theory of mind, central coherence and cognitive shifting) and (4) psychological wellbeing using the symptom checklist (SCL-90). Latent class analysis was applied to delineate whether autistics could be subgrouped according to personality profile.

Results: The scores on the five personality traits of persons with ASD's differ from norm scores, i.e. in general autistics are characterized by high average neuroticism, and low average extraversion, openness, agreeableness & conscientiousness. Applying latent class analysis yielded two personality classes, indicating that about 43% of the subjects (class 1) shows a relatively average personality profile whereas the other 57% (class 2) is characterized by quite pronounced deviations from normscores in the above mentioned directions. Further analyses showed that personality traits & class are related to self-reported autism symptoms and psychological wellbeing: persons in class 2 report more problems than those in class 1, suggesting they represent a more 'vulnerable' group within the ASD population. Personality seems however unrelated to therapist-rated autism symptoms and the three cognitive styles.

Conclusions: The results provide preliminary evidence for the association between personality & experienced suffering from autism symptoms and psychological distress. Longitudinal research is needed to determine the prognostic value of personality regarding general development and treatment success in individuals with ASD.

161.064 64 Co-Occurring Symptoms in a Mixed Clinical Sample of Children with Autism Spectrum Disorders. N. Bilenberg* and M. Paus, *University of Southern Denmark*

Background: Autism spectrum disorders (ASDs) often co-occur with other psychiatric, neurologic, or medical diagnoses. Sub-syndromal problems and even psychotic symptoms are often neglected although these may have almost equally significant impact on the identification, treatment needs, functional status, and progress of children with ASD.

Objectives: This study examined co-occurring problems as rated by parents on the CBCL.

Methods: CBCL data on clinically referred and assessed 6-16-years-old children with ASD (N=110) were compared with equivalent data from age and gender matched typically developed reference children (N=220).

Results: Mean age of the ASD sample was 11.0 (SD 2.6) and 90 % were males. Mean CBCL total

problem score was 61.1 in the ASD sample and 16.8 (SD=14.0) in the reference sample. The most prevalent comorbid problem was rage tantrums in 75 % of cases. Convulsions were 15.2 and obsessions 5.6 times more prevalent in ASD vs. controls. In the ADS group 9.4% were reported as self injurious vs. only 0.9% in the control sample. More results and comparisons will be presented at the conference. Also scores on CBCL subscales with special focus on thought problems and anxiety will be presented and discussed.

Conclusions: These data highlight the need for clinicians to keep in mind the high prevalence of co-occurring problems in combination with an ASD diagnosis. Other symptoms or disorders may mask the core symptoms of ASD and lead to delayed diagnosis. Comorbidity may even be the main focus in tailoring the most effective treatment program.

CBCL is an excellent screening tool in that aspect, before or as an alternative to more comprehensive psychopathological assessment of comorbidity.

161.065 65 Cognitive Task Performance Is Related to ADHD--Not Autistic—Symptomatology in Children with ASD. D. A. Pearson*¹, K. A. Loveland¹, M. G. Aman², C. W. Santos¹, R. Mansour¹, D. M. Lane³, S. Vanwoerden¹, E. Perez⁴, J. Phillips¹, C. Miekka³, T. Dang³ and L. A. Cleveland¹, (1)*University of Texas Medical School*, (2)*Ohio State University*, (3)*Rice University*, (4)*University of Houston College of Education*

Background:

Many children with autistic spectrum disorders (ASD) have significant symptoms of Attention Deficit Hyperactivity Disorder (ADHD), i.e., inattention, hyperactivity, and impulsivity. Given that deficits in cognitive task performance are associated with ADHD in the general pediatric population, children with ASD who have significant ADHD symptomatology may also be at high risk for cognitive task deficits. Using parent and teacher behavioral rating techniques, our group previously demonstrated that parent and teacher ratings of executive function (EF) deficits were related to ADHD--but not ASD--symptomatology in children with ASD. The purpose of this study was to determine if cognitive task performance deficits would also be related

only to ADHD symptomatology—but not autistic symptomatology--in children with ASD.

Objectives:

The purpose of this study was to examine the relationships between 1) cognitive task performance and 2) behavioral ratings of autistic symptomatology and ADHD symptomatology in children with ASD.

Methods:

Participants were 92 children (73 boys; mean age=9.4 yrs.; mean Stanford-Binet 5th Ed. Full Scale IQ=84) who met DSM-IV criteria for ASD on the Autism Diagnostic Interview-Revised (ADI-R) and the Autism Diagnostic Observation Schedule (ADOS). Relationships between the children's cognitive task performance and standardized parent and teacher behavioral ratings of autistic symptomatology (on the Social Communication Questionnaire; SCQ) and ADHD symptomatology (Swanson, Nolan and Pelham Rating Scale, 4th Edition; SNAP-IV) were examined using correlational methods. Cognitive tasks included the Continuous Performance Task (sustained attention and impulsivity), the Speeded Classification Task (selective attention), the Matching Familiar Figures Task (inhibition/impulsivity), and the Delayed Match to Sample Task (immediate memory).

Results:

Children with ASD who had more severe ADHD symptomatology were found to be at significantly higher risk for weaker cognitive task performance, relative to those with milder ADHD symptoms. In contrast, more severe levels of autistic symptoms were not associated with an increased risk of poor cognitive task performance. This relationship between cognitive task performance and behavioral ratings was similar for parent and teacher raters.

Conclusions:

These results extend our previous findings by demonstrating that cognitive task deficits were also strongly related to ADHD severity—but not to ASD severity--in high functioning children with

ASD. Thus, the results of this study provide additional support for the idea that ADHD is manifested in a similar way in children with ASD as it is in the general pediatric population—and that the cognitive task deficits are not associated with the core symptoms of ASD. Rather, these cognitive deficits are manifested in a subset of children with ASD who also have significant ADHD symptoms. Given that cognitive deficits associated with ADHD in the general pediatric population are often successfully treated with medication and/or by behavioral means, cognitive tasks tapping domains such as attention and inhibition may play a helpful role in monitoring ADHD treatment response in children with ASD.

161.066 66 Discriminant and Convergent Validity for the Anxiety Construct in Children with ASD. P. A. Renno*¹ and J. J. Wood², (1)*University of California, Los Angeles*, (2)*University of California Los Angeles*

Background: Children with autism spectrum disorders (ASD) are at heightened risk for developing clinical anxiety. Despite reports of high anxiety in children with ASD there is controversy regarding differential diagnosis of ASD symptoms and anxiety symptoms.

Objectives: To examine evidence of discriminant and convergent validity for anxiety and ASD symptoms in children with ASD.

Methods: This study examined 88 children (63 males), aged 7-11 years, with ASD referred for concerns about anxiety. A multitrait- (social anxiety, separation anxiety, overall anxiety severity, and overall ASD severity), multimethod- (self, parent, and diagnostician) analysis was conducted. Structural equation modeling was used to test for statistical discrimination between anxiety and autism severity and convergence among differing reports of the anxiety subdomains (e.g., separation anxiety).

Results: Findings suggest weak correlations between the ASD and anxiety latent variables (supporting discriminant validity) and moderate to strong loadings of indicator variables on ASD and anxiety latent variables (supporting convergent validity). Model comparisons also provide evidence of statistical discrimination between anxiety and ASD severity and convergence among differing reports of the anxiety subdomains (e.g., separation anxiety).

Conclusions: These results suggest that anxiety symptoms experienced by children with ASD are separate from ASD symptom severity and may instead reflect anxiety syndromes (e.g., separation anxiety) similar to those that occur in typically developing children. Future research using other approaches (e.g. psychophysiology) should be conducted to further investigate ASD and anxiety symptom differentiation.

161.067 67 Do Caregivers and Children/ Youth with Autism Spectrum Disorders (ASD) Agree When Reporting Anxiety Difficulties? A Study Investigating Parent-Child Agreement Using the Spence Children's Anxiety Scale (SCAS). I. Magiati*¹, J. Y. Chan¹, J. W. Tan¹, K. Poon², M. Sung³ and D. Fung³, (1)*National University of Singapore*, (2)*National Institute of Education*, (3)*Institute of Mental Health*

Background: Multiple informants are often employed to obtain more comprehensive and accurate assessment of anxiety difficulties, due to the complex and internalizing nature of anxiety in children. While the utility of the Spence Children's Anxiety Scale (SCAS) as a screening tool for anxiety in typically developing children and youth is well established, little is known with regards to its inter-informant reliability when the scale is used to examine anxiety in children and youth with Autism Spectrum Disorder (ASD). A handful of studies reporting on other anxiety measures with this population have produced mixed findings.

Objectives: The present study aims to examine the utility of the SCAS in providing information on anxiety for children and young people with ASD and will specifically investigate the level of agreement between caregiver and child/ young person.

Methods: Thirty eight caregiver-child pairs were recruited from an autism-specific school in Singapore which admits children with professionally diagnosed ASD *and* non-verbal cognitive scores of >70. All children were aged between 8 to 18 years and completed the SCAS self-report. Caregivers completed the caregiver version of the SCAS. Caregivers also completed the Scales of Independent Behaviour-Revised (SIB-R) in order to provide an estimate of the child's adaptive behavior functioning.

Results: Data have been collected and are currently being analyzed. Parent and child SCAS

correlation analyses will be carried out. To investigate differences between caregiver and child reports of anxiety, Wilcoxon Signed-ranks tests will be carried out between SCAS total and subscale scores from the different informants. Level of agreement will be derived by conducting non-parametric Chi-Square analyses to examine the extent to which clinically significant levels of anxiety as flagged by caregivers where also obtained with children's self-reports.

Conclusions: Preliminary analyses of our findings suggest that inter-rater agreement was low with parents often underreporting anxiety symptoms compared to their children's self-report ratings. Our study findings highlight the high rates of parent-child discrepancy in anxiety ratings and the importance of obtaining information from multiple sources.

161.068 68 Early Phenotype and Developmental Trajectories of Children with ASD with and without Comorbid ADHD. P. Rao* and R. Landa, *Kennedy Krieger Institute*

Background:

A growing number of researchers are reporting symptoms of Attention Deficit/Hyperactivity Disorder (ADHD) in a substantial proportion of children with ASD (e.g., Mayes, Calhoun, Mayes, & Molitoris, 2012). There is preliminary evidence that when ADHD is comorbid with ASD, the risk for a more severe behavioral phenotype increases (Holtmann et al., 2007; Rao & Landa, in press; Yerys et al, 2007). A major need in the field of autism research is to better understand whether early phenotypic characteristics and trajectories of children with ASD who develop comorbid ADHD differ from those without ADHD comorbidity.

Objectives:

To determine whether early developmental differences exist in cognitive functioning, language acquisition, ASD symptom severity in children with ASD who were identified at school-age as having comorbid ADHD or no ADHD comorbidity.

Methods:

Participants were 44 children (ages 4-8 years) with ASD participating in a prospective study of

child development. Data were collected at ages: 24 months (T1); 36 months (T2); and 4 to 8 years (T3). At T3, parent ratings on the BASC-2 were used to classify children as ASD-Only ($n = 29$) or ASD+comorbid ADHD ($n = 15$). The Mullen Scales of Early Learning (MSEL) age equivalency scores were used at T1 and T2 to assess nonverbal cognitive (Visual Reception [VR] scale) and language functioning (Expressive Language [EL] and Receptive Language [RL] scales). Age equivalents from the Peabody Picture Vocabulary Test-P3, and the Oral Vocabulary subtest of the Test of Oral Language Development-P3 were measures of receptive and expressive language at T3. Severity of ASD symptoms was measured with the Autism Diagnostic Observation Scale (ADOS) at Ts1-3.

Results:

Independent samples t-tests revealed no significant between-group differences in gender, ethnicity, recruitment source, or age of assessment at T3 (Table 1). One-way ANOVA revealed that the ASD+ADHD group had significantly lower nonverbal IQ than the ASD Only group at T1 ($F = 4.78, p = .04$) and T2 ($F = 9.87, p = .003$). Similarly, expressive language at T1 ($F = 4.65, p = .04$) and T2 ($F = 6.11, p = .02$), and receptive language at T2 ($F = 9.12, p = .004$) and T3 ($F = 4.71, p = .04$) were more impaired in the ASD+ADHD group than in the ASD-Only group. There were no significant between-group differences in severity of ASD symptoms at any time of assessment (see Figure 1).

Conclusions:

Findings indicate that, by the toddler years, children with ASD who later exhibit clinically significant ADHD symptoms present with more severe cognitive and language phenotypes than those without comorbid ADHD symptoms. Future studies replicating and expanding upon these findings are needed so that early interventions targeting this specific behavioral phenotype may be developed.

161.069 69 Emotions and Aggression in Young Adolescents with an Autism Spectrum Disorder; A Longitudinal Study. C. Rieffe*¹, L. B. Pouw¹, E. Broekhof¹ and L. Stockmann², (1)Leiden University, (2)Centrum Autisme Rivierduinen

Background:

Aggressive behaviors have been frequently observed in children with Autism Spectrum Disorder (ASD), but little research has been done to determine possible motives and causes of these behaviors. Poor emotion regulation skills could be causing these aggressive behaviors. Clinicians sometimes argue that aggressive behaviors in children with ASD should not be interpreted the same way as in typically developing (TD) children. In TD children, a lack of empathy is associated with higher levels of aggression. Although children with ASD are known for their atypical empathic development, it has never been studied in relation to their aggressive behavior. Therefore, in this study, the main aim was to examine longitudinally the causal relationship between emotion regulation, empathy and aggression in young adolescents with ASD, as compared to their TD peers,

Objectives:

The main aim of this study was to examine the extent to which impaired capacity for emotion regulation and empathy would be causally related to more aggression, and whether these associations differed between young adolescents with ASD and TD adolescents,

Methods:

The study included 133 adolescents (67 ASD, 66 TD, mean age 11 years, 7 months), who filled out self-report questionnaires on aggression, anger, and empathy. Data were collected 3 times, with a 9 month time-interval,

Results:

Cross-sectional analyses of the first data wave show that anger was related to more reactive and proactive aggression in young adolescents with ASD and in the TD control group. Yet, affective empathy was related to less reactive aggression in TD children, as expected, but to more reactive aggression in young adolescents with ASD,

Conclusions:

The outcomes of this study support the idea that distress in others evokes over-arousal in young adolescents with ASD. This, in turn, causes aggressive behaviours, due to a combination of poor emotion regulation and impaired understanding of the emotions of others. The longitudinal data will be analysed for this presentation and allow us to discuss the extent to which the assumptions made on causality between emotion regulation and aggression will hold.

161.070 70 Empirically Established Typologies of Co-Morbid Disorders in Adolescents with ASD. B. L. Baker*¹, J. Blacher², C. Neece³ and B. Caplan¹, (1)UCLA, (2)University of California, (3)Loma Linda University

Background: There is growing recognition that emotional and behavioral problems are common among youth with ASD. Indeed, some have argued that co-morbidity in this population may be the rule rather than the exception (Gillberg & Billstedt, 2000). Our knowledge about co-morbidity is hampered, however, by several factors. First, many studies utilize only one diagnostic instrument to determine co-morbidity; there is variability in findings from different instruments. Second, many studies do not control for concomitant ID in populations with ASD, thus confounding the actual risks. Third, many studies do not include a comparison group with neither ID nor ASD. Thus, we need further controlled research examining the clinical presentation and consequences of dual diagnosis among youth with ASD.

Objectives: We will present two related papers. This first will report findings about behavior problems and mental disorders in adolescents with ASD, and compare these to rates from adolescents with typical development or ID. The second will examine the collateral effects of comorbid mental health disorders on domains of family functioning.

Methods: This research is drawn from the Collaborative Family Study, a three-university longitudinal study of mental disorders in children with or without ID. We report findings from age 13 assessments, when we added a sample of youth with ASD. The current sample, N=195, contains youth with typical development (IQ >84) and no ASD (n=100), High Functioning Autism (IQ>85; n=29), and ID with (n=27) or without

(n=39) comorbid ASD. The primary measures of behavior problems/mental disorders were the Child Behavior Checklist (questionnaire) and the Diagnostic Interview Schedule for Children (interview).

Results: A consistent finding is that for youth without ASD, IQ correlates significantly with every measure of behavior/mental disorders; the lower the IQ, the greater incidence of disorder. Conversely, for youth with ASD, the IQ level does not correlate significantly with any measure of behavior/mental disorders. Youth with ASD tend to be higher in the incidence of co-morbid disorders, regardless of intellectual functioning. We found similar heightened problems for youth with ASD (vs. no ASD) on CBCL externalizing and internalizing scales, and clinical scales assessing ADHD, ODD, Affective disorders, and Anxiety disorders. Again we found similar findings on the DISC domains of ADHD (inattentive and hyperactive types) and ODD. In most cases, there was also a significant effect of intellectual disability (vs. no ID) and in some cases an interaction.

Conclusions: It appears that, in terms of percentages reaching a diagnostic cut-off, youth with ASD and/or ID are about three times as likely to meet criteria for a disruptive behavior disorder as youth without either diagnosis. We have considered elsewhere whether a disorder (e.g. ADHD) in youth with ID is simply a reflection of ID characteristics, or represents a separate disorder (similar to ADHD in typically developing youth) that is over and above the ID (Baker et al., 2010; Neece et al., 2012). We will address this same diagnostic question in reference to disorders in youth with ASD.

161.071 71 Examining Behaviour and Emotional Problems in Preschool Children with Developmental Delay. K. M. Gray*¹, J. R. Taffe¹, C. Keating¹, D. Sweeney¹, S. L. Einfeld² and B. J. Tonge¹, (1)Monash University, (2)University of Sydney

Background: Research has established that behaviour and emotional problems occur at a significantly high rate young people with intellectual disability and decline slowly over time. These behaviour and emotional problems occur at even higher rates in children with Autism Spectrum Disorders. Comparatively less is known about the nature and presentation of such

difficulties in preschool children with developmental delay.

Objectives: This study aimed to develop a psychometrically robust measure to examine behaviour and emotional problems in preschool children with developmental, including autism. A secondary aim involved exploration of the range of behaviour and emotional problems in and the association with parent psychosocial distress.

Methods: The first stage of this study involved the development of a measure designed specifically to examine behaviour and emotional problems in preschool children with developmental delay. This measure, the Developmental Behaviour Checklist-Under 4 (DBC-U4), was then used to examine behaviour problems in a community sample of children aged 18-48 months, with or suspected of developmental delay. Reliability and validity were comprehensively evaluated in samples of mothers (n=286), fathers (n=228), and teachers (n=101). Presentation of child behaviour and emotional problems in preschool children were explored, along with associations with maternal and paternal psychosocial distress.

Results: Data will be presented on the reliability, validity, and factor structure of the new measure in a sample of 290 children aged 18-48 months. Information on the rate and presentation of child behaviour problems, along with associations with age, gender and developmental level will be presented. The relationship between child behaviour problems and maternal (n=286) and paternal (n=228) psychosocial distress will also be explored.

Conclusions: The DBC-U4 provides extensive range of information on different symptoms and difficulties experienced by young children with developmental difficulties. It provides an means to identify behaviours to target in interventions, track response to interventions, identify the need for further assessment (e.g. for autism), and inform the support needs of parents and families. From a clinical research perspective, this new measure can assist in developing a greater understanding of the presentation of behaviour and emotional problems in early childhood, and thus facilitate the development of specific early interventions. This may also provide insight into the origins of severe behaviour and emotional

problems that can be observed in later childhood and adolescence.

161.072 72 Examining the Relationship Between Parental Substance Use, Child Problem Behaviors, and the Broad Autism Phenotype. J. L. Wade*, N. B. Cox, R. E. Reeve and M. F. Hull, *University of Virginia*

Background: Parents of children with Autism Spectrum Disorders (ASDs), particularly those whose children exhibit severe externalizing behaviors, report higher levels of stress than not only parents of typically developing children, but also parents of children with other developmental delays. Stress makes everyone, including parents, more vulnerable to the adoption of maladaptive coping strategies, which can include substance use; parental substance use is particularly concerning given its potential impact on the parent-child interaction, as well as parents' perceptions of their children. Despite the unique stressors faced by parents of children with ASDs, to the researchers' knowledge, parental substance use among this population has not been studied. Based on the current literature, the researchers hypothesize that parents of children with ASDs may utilize substances as a coping mechanism; the parents of children who engage in severe externalizing behaviors may be at even greater risk. Furthermore, research indicates that parents with phenotypes associated with ASDs, also known as the Broad Autism Phenotype (BAP), are more likely to adopt maladaptive coping mechanisms, which may translate to increased substance use.

Objectives: The present study seeks to define the prevalence of substance use among parents of children with ASDs, as well as determine whether or not there is a relationship between parental substance use and the severity of their children's problem behaviors as reported on the Externalizing subscale of the Child Behavior Checklist (CBCL). Furthermore, this study aims to determine whether or not parents engaging in substance use register on the Broad Autism Phenotype as measured by the subscales and overall average score on the Broad Autism Phenotype Questionnaire (BAPQ).

Methods: Data for this study were obtained from the Simons Simple Collection (SSC). The following measures were used: Child Behavior Checklist, Broad Autism Phenotype Questionnaire, and the

Parent Substance Use History Form (developed by the SSC). For the purposes of this study, only current substance use data were analyzed. Given that parental substance use is a dichotomous variable (as measured by the SSC), point-biserial correlations were run between parental substance use, the CBCL Externalizing subscale, and the subscales and overall average score of the BAPQ. Paternal and maternal substance use data were analyzed separately.

Results: With the exception of tobacco and alcohol use, a relatively small percentage of parents reported substance use; however, preliminary analyses yielded significant correlations between parental (paternal and maternal) substance use and BAPQ scores.

Conclusions: These findings suggest that parents exhibiting BAP traits may be more likely to adopt maladaptive coping mechanisms, specifically substance use. Although effect sizes were relatively small, these results suggest important implications for future research. To enhance our understanding of the data, the researchers plan to conduct additional analyses by looking at the relationships between the BAPQ and the CBCL and composite scores of substance use (for both mothers and fathers), which will be included in the conference presentation.

161.073 73 Examining the Similarities and Differences in Behavioral and Emotional Problems in Children with Autism Spectrum Disorders and Those Diagnosed with Anxiety Related Disorders. S. J. Weng^{*1}, M. Sung¹, M. Raja¹, S. Sung¹, L. Y. Jang¹, D. S. S. Fung² and Y. P. Ooi³, (1)*Institute of Mental Health*, (2)*Nanyang Technological University*, (3)*University of Basel*

Background: Autism Spectrum Disorders (ASD) is a debilitating neurodevelopmental condition characterized by deficits in core areas such as social interaction and communication, and is often accompanied by restricted and repetitive behaviors and/or interests. Individuals with Generalized Anxiety Disorder (GAD) and Selective Mutism (SM) may often share various forms of social deficits like impaired social behavior and social cognition. Additionally, anxiety often co-occurs with ASD and authors have posited that a host of difficulties in ASD may arise from the fact that these individuals find social interaction unpredictable and anxiety provoking.

Objectives: This study aims to characterize the profiles of individuals with ASD, SM and GAD using the Child Behavioral Checklist (CBCL) and to examine the similarities and differences in behavioral/emotional problems manifested by these clinical populations.

Methods: A total of 80 participants between the ages of 6-19 years old, who received a diagnosis of ASD, GAD or SM were recruited from the Child Guidance Clinic, an outpatient clinic of the Institute of Mental Health in Singapore. Demographic information and medical history was collected and parents were asked to complete the Child Behavioral Checklist (CBCL) (Achenbach & Rescorla, 2000, 2001), a 118-item parent questionnaire that provides information on the child's behavior and emotions. A one way ANOVA was conducted in order to examine group differences on the subscales of the CBCL.

Results: Preliminary results revealed that there were group differences in some of the subscales scores of the CBCL. Specifically, the categories were: anxious/depressed $F(2, 78) = 11.27, p < 0.0001$; withdrawn/depressed $F(2, 78) = 6.27, p = 0.003$; attention problems $F(2, 78) = 5.52, p = 0.006$ and somatic complaints $F(2, 78) = 4.87, p = 0.01$. Post-hoc analysis revealed that the GAD group scored significantly higher on the anxious/depressed syndrome scales than the SM and the ASD group. The SM group scored significantly higher on the withdrawn/depressed syndrome scales than the GAD and ASD group. The ASD group scored significantly higher on the attention problems scale than the SM group and finally, the GAD group scored significantly higher on somatic problems scale than the SM group.

Conclusions: These preliminary results suggest that the GAD group had higher levels of anxiety symptoms than both the ASD and the SM groups. Additionally, the GAD group had higher levels of somatic problems than the SM group. On the other hand, the SM group had reportedly higher levels of withdrawn/depressed symptoms than the GAD and ASD groups. Finally, the ASD group had higher levels of attention problems than the SM group. These findings suggest some evidence for areas of divergence between disorders which share some similar deficits. The characterization of behavioral and emotional problems in this study contributes to our knowledge of these

disorders and can help to lay the groundwork for refining future treatments within these clinical populations.

161.074 74 Exploring the Agreement Between Dimensional CBCL Measures and Categorical DSM-IV Diagnoses of Comorbid Psychopathology in Children with Autism Spectrum Disorders. E. Gjevik*, *University of Oslo*

Background:

Autism spectrum disorders (ASD) are often comorbid with other psychiatric symptoms and disorders. However, identifying and describing psychiatric comorbidity in children and adolescents with ASD is challenging.

Objectives:

To explore how a dimensional questionnaire, The Child Behaviour Check List (CBCL), agreed to a DSM-IV based standardized interview, The schedule of Affective Disorders and Schizophrenia (Kiddie-SADS), in identifying comorbid psychiatric symptoms and disorders, and explore the usefulness of combining these two diagnostic tools in clinical practice.

Methods:

The study sample included a clinically representative group of 55 children and adolescents with ASD, ranging in age from 6 to 18 years, including the three main ASD subgroups and the broad range of cognitive and language functioning. Questionnaire and interview assessment were based on parent information

Results:

High rate of psychopathology was found both through questionnaire and interview assessment. Thirty-eight children (69% of the sample) had elevated scores on the CBCL Thought problem scale, 35 (65%) on the Attention Problems scale and 34 (62%) on the Affective Problems scale. Forty children (73%) were diagnosed with at least one comorbid DSM-IV disorder. ADHD (17 children, 31%) and anxiety disorders (24 children, 40%) were the most prevalent. We found good agreement between the CBCL and the Kiddie-SADS for identifying children with comorbid ADHD, depressive disorder and OCD. However, a

high number of children had elevated CBCL scores, but no interview identified ADHD, depressive disorder or ODD/CD. There was poor agreement between the CBCL and the Kiddie-SADS for identifying children with anxiety disorders.

Conclusions:

This explorative study is one of very few directly comparing dimensional questionnaire information and categorical DSM-IV diagnoses of comorbid psychopathology in children and adolescents with ASD. Our findings support the use the CBCL for identifying children with comorbid DSM-IV defined ADHD, depressive disorder and ODD/CD, but not for identifying children with anxiety disorders. The CBCL questionnaire seems to capture core symptoms of ASD as well as comorbid psychopathology, and clinicians should be aware that the CBCL may be unspecific when used in children with ASD.

161.075 75 Factor Structure and Measurement Invariance of the Spence Children's Anxiety Scale - Parent Version Across Anxious and ASD Groups. M. Glod*¹, J. Rodgers¹, M. South², S. A. Baldwin², C. Creswell³ and H. McConachie⁴, (1)*Newcastle University*, (2)*Brigham Young University*, (3)*University of Reading*, (4)*Institute of Health and Society, Newcastle University*

Background: Anxiety, is a common health concern in children with autism spectrum disorder (ASD) affecting between 11% and 84% (White et al. 2009) compared to 3-24% of typically developing children (Green and Ben-Sasson 2010). The Spence Children's Anxiety Scale-Parent Version (SCAS-P; Spence 1998) is a commonly used parent-report instrument for assessing anxiety (Nauta et al. 2004) and has been used with children and young people on the autism spectrum (Chalfant et al. 2006; Russell and Sofronoff 2005, Rodgers et al. 2012). However, the SCAS-P was developed with typically developing children and there is very little information available regarding the validity of the SCAS-P for use with ASD samples. The measure is frequently used to compare anxiety in children with ASD to other groups and further investigation is required to be confident that the scale functions in the same way across groups.

Objectives: The aims of this study were:

- to determine then compare the factor structure for the SCAS-P in a sample of young people with ASD and a sample of anxious young people,
- to use measurement invariance techniques to determine whether SCAS-P items function in the same way and are on the same metric in children with ASD and children with anxiety in order to suggest whether cross-groups comparisons using the SCAS-P are appropriate and meaningful.

Methods: Parents of 232 children with ASD aged between 8 and 16 years, and 163 children without ASD with a current anxiety disorder aged between 7 and 15 years, completed the SCAS-P. Confirmatory Factor Analysis (CFA) was undertaken in order to determine the best-fitting factor structure. Measurement invariance was performed in order to establish whether structure, factor loadings, item intercepts and error variance were same across groups.

Results: A five-factor model with the Generalized Anxiety Disorder subscale excluded was found to be the best-fitting factor structure in both groups. Configural and metric measurement invariance showed that the general model structure was invariant across groups, but non-invariance was found to be present for factor loadings between groups, terminating further analysis. Additional Exploratory Factor Analysis (EFA) indicated that the items loading on the physical injury fears factor differed between groups, with stronger loadings in the anxious group than in the ASD group.

Conclusions: Factor analyses determined that the five-factor model (excluding GAD subscale) fit the data best. Anxiety as a concept, measured with the SCAS-P, is not identical across the two groups. Cross-group comparisons between children with ASD and children diagnosed with anxiety disorder based on the SCAS-P scores should therefore be undertaken with caution. The SCAS-P norms established for anxiety disordered children may not be appropriate for individuals with ASD. Qualitative work is needed to explore the validity of some SCAS-P items in the ASD population.

161.076 76 Five-Year Follow-up of Preschoolers with Autism and Comorbid Psychiatric Disorders. J. Kim, S. F. Freeman, T. Paparella* and S. R. Forness, *UCLA*

Background: Studies have reported the prevalence of total comorbid psychiatric disorders in children with autism spectrum disorders (ASD) to be from 30-80%. Such comorbid conditions are thought to not only exacerbate the social, communicative and behavioral difficulties already inherent in children with autism but also to complicate diagnosis and access to services. Despite these concerns there are no current longitudinal studies of such children regarding the impact of comorbidity.

Objectives: To assess the nature and occurrence of comorbid psychiatric symptoms in children with ASD 5.5 years after their initial diagnosis and treatment in preschool. The study focuses on the nature and extent of psychotropic medications, special education and related behavioral or mental health services potentially warranted by comorbid disorders.

Methods: One hundred and seventy five participants with a confirmed autism diagnosis were assessed at entry to an early intervention program (time 1). Comorbid symptoms were assessed using the Early Childhood Inventory (ECI) - 4: Parent Checklist and Child Behavior Checklist (CBCL). The Mullen and Wechsler Primary Preschool Scales of Intelligence-III (WPPSI) were used to assess intellectual functioning and to derive a mental age for each child. After 5.5 years (time 2), 44 preschoolers were located and reassessed for comorbid disorders at an average chronological age of 10 years 3 months. Comorbid symptoms were re-assessed using the Child or Adolescent Symptom Inventory - 4: Parent Checklist and the Child Behavior Checklist. A subsample of 25 families was interviewed regarding their child's current special education programs and the types of behavioral or mental health services they were currently receiving. Careful analyses were used throughout to ensure the representativeness of the samples.

Results: Comorbidity persists in similar patterns five years after initial symptoms with the time 1 ranking as follows: ADHD, depression, dysthymia, anxiety; and the time 2 ranking as: dysthymia,

ADHD, depression, anxiety. Preschool mental age predicts both mood and anxiety disorders. By around 5th grade, 64% were in regular class (1/3 with aides). Related services (hours/week) were: behavioral aide (17), social skills (1.5), speech therapy (1.5), and mental health services (0.3). Psychotropic medications were used by 73% of children at time 1 and 61% at time 2. Externalizing symptoms improved more than internalizing symptoms.

Conclusions: Findings not only suggest continued comorbidity but also somewhat higher than expected use of behavioral services, often requiring out of school funding. Dysthymia was the only disorder that significantly worsened over time suggesting that identification of and treatment of at least some comorbid internalizing disorders may be sorely lacking in school settings for children with ASD. Hours per week devoted to behavioral aides and primacy of medication for ADHD or disruptive behavior contrasted sharply with services such as counseling or related mental health services that might be more likely to target internalizing problems. Comorbid externalizing disorders, such as ADHD, seemed to fare a little better, possibly because special education and related services tend to focus on externalizing disorders.

161.077 77 Follow-up of Maladaptive Behaviors in Youth with Autism Spectrum Disorders: Changes and Predictors Over Two to Eight Years. M. Chowdhury*¹ and M. G. Aman², (1)*Allegheny College*, (2)*Ohio State University*

Background: Ample evidence suggests that young people with autism spectrum disorders (ASDs) present with maladaptive behaviors beyond the core symptoms defining the disorder. Such behaviors represent additional impairments and are associated with increased caregiver stress. In spite of their prevalence and significance, the natural course of maladaptive behaviors is not well delineated in the ASD literature.

Objectives: We conducted a follow-up study to: (1) Examine the *stability* of and *changes* in maladaptive behaviors in a sample of children and adolescents with ASDs from initial contact (T1) to follow-up (T2); (2) Assess variables that might predict maladaptive behavior levels at T2.

Methods: Participants were recruited using patient records at an UCEDD-affiliated diagnostic clinic, where potential participants were given an ASD diagnosis two-to-eight years previously. All individuals seen had a measure of maladaptive behavior on file, assessed using the Nisonger Child Behavior Rating Form (NCBRF; Aman, Tassé, Rojahn, & Hammer, 1996). We conducted follow-ups on 342 potential participants and collected data from 143 of these individuals (41.8% response rate). Follow-up data included current parent-rated NCBRF and supplementary demographic information.

Results: The final sample ranged in age from 5 to 17 years at follow-up. Results from paired *t*-tests indicated significant differences between T1 and T2 NCBRF scores for all six subscales. Scores on three of the subscales (*Conduct*, *Hyperactivity*, and *Self-injury/Stereotypic*) showed significant *improvement* over time. Scores on the remaining three subscales (*Insecure/Anxious*, *Self-isolated/Ritualistic*, and *Overly Sensitive*) *deteriorated* at follow-up. Interestingly, a significantly greater proportion of those with Asperger's disorder and PDD-NOS (as compared to autism) deteriorated on these subscales.

Using units of 0.50 *SD* to denote improvement, no change, and worsening (Shattuck et al., 2007), the greatest proportion of participants were found to improve on *Hyperactivity* (61.5%), followed by *Conduct* (43.3%). The highest proportion worsened on *Self-isolated/Ritualistic* (66.4%), followed by worsening on *Insecure/Anxious* (58%). Scores on *Self-injury/Stereotypic* were the most stable over time with 67.8% of participants showing no change. Levels of maladaptive behaviors varied considerably based on gender, ASD subtype, and language abilities of participants.

As far as *predictors* of maladaptive behavior change, results from a series of hierarchical regression analyses indicated that tested models accounted for 39% to 50% of the variance in T2 NCBRF subscale scores. T1 scores on the respective NCBRF subscales were the most consistent predictors of scores at follow-up, suggesting that a child's individual levels of T1 maladaptive behavior were the best predictor of maladaptive behavior over time. Other variables that significantly predicted T2 scores on one or

more NCBRF subscales included T1 age, ASD subtype, and T1 language ability.

Among other salient findings, parents reported high rates (68.5%) of comorbid psychiatric conditions in this community sample unselected for psychiatric disorders and also a high rate of psychotropic medication use (52.4%). The most common comorbid disorders were anxiety disorders (37.8%) and ADHD (31.5%).

Conclusions: Findings from this study provide additional clarification on the natural course of maladaptive behavior in ASDs and have implications for clinicians, parents, and service providers in anticipating change over time and planning interventions.

161.078 78 Formal Thought Disorder in Children with Autism Spectrum Disorder: Indicator of Future Psychotic Symptoms or Indicator of Severe Autistic Symptoms. A Seven Year Follow up Study. M. Eussen^{*1}, E. I. de Bruin², A. R. Van Gool³, S. C. Louwse⁴, F. Verheij⁵, F. C. Verhulst⁶ and K. Greaves-Lord⁶, (1)*Yulius Mental Health Organization*, (2)*University of Amsterdam*, (3)*Yulius Academy*, (4)*Erasmus MC - Sophia*, (5)*Sophia Children's Hospital*, (6)*Erasmus MC - Sophia's Childrens Hospital*

Background: Formal Thought Disorder (FTD) is a disruption in the flow of thought, which is inferred from the disorganization of spoken language and which is a manifestation of severely disturbed language processing. FTD was once considered to be the hallmark of psychotic disorders, but nowadays it is considered as an important symptom of autism spectrum disorders (ASD) as well. FTD in childhood might be a developmental precursor of psychotic disorders or a manifestation of more severe impairment in ASD.

Objectives: The current longitudinal study is a seven year follow-up on 91 individuals with ASD, and it was investigated 1) whether symptoms of FTD during childhood predicted prodromal symptoms of psychosis in adolescence, and 2) whether symptoms of FTD during childhood were associated with higher ASD symptom severity in adolescence.

Methods: ASD symptom severity was assessed in childhood (T1) and seven years later in adolescence (T2), using the Autism Diagnostic Observation Schedule (ADOS). At T1, the Kiddie-

Formal Thought Disorder Scale (KFTDS) was used to measure symptoms of FTD. At T2, the Prodromal Questionnaire (PQ) was used to assess (pre)psychotic symptoms.

Results: FTD symptoms at T1 did not predict prodromal symptoms of psychosis at T2. FTD symptoms at T1, especially loose associations predicted severity of autism spectrum disorder at T2 over a period of 7 years.

Conclusions: FTD predicts more severe symptoms of ASD over a period of seven years and appears to be a manifestation of more severe impairment in ASD, but does not predict prodromal symptoms of psychosis.

161.079 79 Genetic and Environmental Components of the Relationship Between the ASD Triad and Mental Health Problems Measured by Strengths and Difficulties Questionnaire (SDQ). B. Tick^{*}, F. Rijdsdijk, F. McEwen and F. Happe, *SGDP, IoP, King's College London*

Background: Autism Spectrum Disorders (ASD) has a higher prevalence rate than thought before: ~0.6% to 1% in children as well as adolescents (Baird et al., 2006). In addition, the presence of other psychiatric disorders in children with ASD is becoming increasingly recognised (Simonoff et al., 2008). It is, however, not clear why these disorders covary and researchers are trying to understand the nature and origin of the elevated rates of psychiatric diagnosis in ASD sufferers.

Objectives: The aim is to examine the genetic and environmental overlap between the distinct parts of the ASD triad (social interaction, communication and rigid and repetitive interests) and other psychiatric difficulties as measured by the Strengths and Difficulties Questionnaire (SDQ). SDQ measures emotional and conduct problems, hyperactivity/inattention, peer relationships and prosocial behaviour. The sample is an existing selected twin dataset sourced from Twins Early Development Study (TEDS).

Methods: The genetic and environmental overlap between ASD and SDQ will be tested using a bivariate threshold liability model consisting of MZ and DZ concordant/discordant ASD pairs as well as controls. To control for the fact that the sample is selected for ASD diagnosis, we fix the ASD parameters to population known values. Then,

using the ratio of MZ:DZ cross-twin & cross-trait correlations of ASD and SDQ we estimate the genetic and environmental correlations to examine the aetiology of the comorbidity between these two traits. This method proved successful in the past for detecting comorbidity between schizophrenia and associated endophenotypes and is described in detail elsewhere (Rijsdijk et al., 2007).

Results: Preliminary results for the composite SDQ show a phenotypic correlation with ASD of .38. This covariance was largely due to overlapping genetic influences (71%) with the remaining 29% of the covariance due to non-shared environmental influences. Similarly, using the emotional subscale of SDQ, we report phenotypic correlation of .37, 67% of covariance is explained by genes and 30% by non-shared environments.

Conclusions: The current results indicate pleiotropic genetic effects influencing both the genetic liability to ASD and other psychiatric difficulties.

161.080 80 HRV As a Measure of Arousal in Social Interaction for Individuals with ASD. L. Guy*¹, L. E. Bradstreet², C. M. DeLussey¹, L. Le¹ and J. D. Herrington³, (1)*The Children's Hospital of Philadelphia*, (2)*Georgia State University*, (3)*University of Pennsylvania*

Background:

Heart Rate Variability (HRV; the rhythmic beat-to-beat change in heart rate) has been used as an indicator of emotional regulation and psychological adjustment in numerous studies (Beauchaine, 2001). It has recently been used to better understand the social deficits seen in ASD. The polyvagal theory (Porges, 1998, 2011) describes a neural social engagement system, and the functioning of this system can be measured by assessing the action of the vagal nerve on the heart, which manifests as HRV. Higher HRV indicates more parasympathetic activity, which in turn reflects better emotional regulation and a readiness to engage in social interaction. The polyvagal theory predicts that individuals with ASD would have lower HRV during reciprocal social interactions.

Objectives:

The first aim of this study was to compare HRV for individuals with ASD to neurotypical controls (TDC) across the conditions of resting baseline, a live socially demanding task (i.e., conversation task from the ADOS), and a cognitively demanding task (i.e., Matrices subtest from the DAS-II). The second aim of the study was to investigate the relationship between HRV and parent-report measures of emotional regulation (i.e., Emotional Control subtest of the BRIEF), anxiety (i.e., the SCARED), and socialization skills (i.e., the Socialization subtest of the VABS-II).

Methods:

The groups included 18 individuals with ASD and 20 control individuals (TDC) that were matched for age and overall IQ. The diagnosis of ASD was confirmed using the ADI-R and ADOS, and IQ was assessed using the DAS-II. The Biopac MP150 system and BioNomadix Respiration & ECG Modules were used at a sampling rate of 1000 Hz. ECG data were collected using a standard Lead-II configuration with disposable electrodes, and respiration was measured via a small belt (strain gauge) fastened lightly around the sternum. After placement of the electrodes and respiration belt, participants were seated at a table across from the examiner. The task presentation was counterbalanced and included baseline, socially demanding task, baseline, cognitively demanding task, and baseline, with each task lasting for 6 minutes.

Results:

There were no significant differences in age between the ASD ($M=11.77$, $SD=3.00$) and TDC ($M=13.18$, $SD=3.15$) groups; $t(36)=-1.40$, $p=.168$. Additionally, there were no significant differences in overall IQ between the ASD ($M=104.28$, $SD=20.70$) and TDC ($M=105.45$, $SD=10.40$) groups; $t(36)=-.22$, $p=.824$. HRV data were analyzed using power spectral analysis of the high frequency range of .12-1.0 Hz. Preliminary analyses of the HRV data indicated significant group differences for the initial baseline condition. Additional analyses are ongoing.

Conclusions:

A strength of this study is the assessment of HRV during a live social interaction, which enhances the ecological validity of the findings. Although data analysis is in preliminary stages, the identification of emotional arousal (lower HRV) during social interactions for individuals with ASD may have important treatment implications since most interventions involve a social component. Including strategies to increase HRV (e.g., stimulating and exercising the neural pathways of the social engagement system) may allow individuals with ASD to profit more from the interventions they are receiving.

161.081 81 Heart Rate Variability and Anxiety in Autism Spectrum Disorders. L. Le*¹, I. Giserman¹, V. Y. Chow¹, L. N. Berry², C. M. DeLussey¹, L. Guy¹ and J. D. Herrington³, (1)*The Children's Hospital of Philadelphia*, (2)*Baylor College of Medicine*, (3)*University of Pennsylvania*

Background: Anxiety is a frequently occurring comorbid condition of Autism Spectrum Disorders (ASD), with prevalence rates estimated to be approximately 40% or higher in some studies. As most anxiety measures are heavily loaded on verbal abilities, there is a substantial need for non-verbal indices of anxiety in ASD. Peripheral nervous system function may ultimately provide a language-free index of arousal dysregulation in ASD—one that has been linked to anxiety disorders in typically developing populations. In anxiety disorders, dysregulation of the parasympathetic nervous system (i.e., abnormal vagal tone) has been associated with an inability to adjust appropriately and quickly to environmental changes and stressful challenges (Beauchaine et al., 2007). One way to measure physiological dysregulation is with Heart Rate Variability (HRV), defined as the rhythmic beat-to-beat change in heart rate. Conversely, greater HRV is associated with superior adaptability and autonomic regulation to stressors. The present study examines the relationship of HRV and anxiety in ASD.

Objectives: The aim of this study was to evaluate differences in HRV among children with ASD and comorbid anxiety, ASD alone, and TDC, when viewing 8 minutes of static and 8 minutes of dynamic sets of images of neutral, happy, and angry facial expressions. Angry faces have been shown to elicit an anxiety response in both neurotypical and ASD populations.

Methods: Participants were assessed for ASD and anxiety using gold-standard instruments: ADOS, ADI-R, and ADIS. Cognitive ability was evaluated with the DAS-II. HRV and respiration were recorded using the Biopac MP150 Respiration & ECG Modules, sampled at 1000 Hz and analyzed using power spectral analysis to determine power in the high frequency range of 0.12-1.00Hz. Participants were seated in a comfortable chair and static and dynamic facial stimuli were presented on a computer screen for 8-minute sessions. Response data was also recorded after each trial where participants pressed a button to discriminate neutral, happy, and angry facial expressions.

Results: 46 participants (33 ASD, 13 TDC) completed both the face tasks and the anxiety disorder diagnostic battery. Of the 33 individuals with ASD, 20 met criteria for at least one anxiety disorder, yielding three groups: ASD with anxiety, ASD only, and TDC (who were preselected to be free of Axis I psychopathology). An ANOVA showed no group differences within the three groups on age; $F(2,45)=0.125, p=.0.883$ (mean age in years=11.51, 11.05, 11.46, respectively) and IQ; $F(2,45)=2.184, p=0.125$ (DAS-II GCA; mean IQ=99.05, 110.92, 113.85). Data analysis is ongoing.

Conclusions: Although data analysis for this study is in preliminary stages, this study contains one of the first ASD samples that have been well-characterized in terms of both anxiety disorder status and parasympathetic nervous system function. Data from this study will fill a gap in our understanding of the psychophysiology of anxiety in ASD. Ultimately, measures of autonomic flexibility such as HRV may provide insight into how individuals with ASD and co-occurring anxiety manage the affective elements of interpersonal situations.

161.082 82 Inattention and Hyperactivity in Association with Autism Spectrum Disorders in the CHARGE Study. K. Lyall*¹, J. Schweitzer², M. Solomon², R. J. Schmidt² and I. Hertz-Picciotto³, (1)*University of California, Davis*, (2)*University of California, Davis M.I.N.D. Institute*, (3)*UC Davis M.I.N.D. Institute*

Background:

Symptoms of attention deficit hyperactivity disorder (ADHD) are common in individuals with

autism spectrum disorders (ASD), but it is not clear how these issues manifest in young children or how they correlate with other features of autism.

Objectives:

To compare inattention and hyperactivity symptoms as measured by the Aberrant Behavior Checklist (ABC) in young children with ASD, developmental delay (DD) without ASD, and typical development (TD), and to characterize attention deficits in ASD. In particular, we explored whether these behaviors were related to child cognitive and behavior scores, demographic factors, and selected environmental risk factors previously associated with ASD.

Methods:

Participants were children 3-5 years of age, who were enrolled in the Childhood Autism Risks from Genetics and the Environment (CHARGE) population-based case-control study. TD and DD control groups were defined according to scores on the Social Communication Questionnaire (SCQ), Mullen Scales of Early Learning (MSEL), and the Vineland Adaptive Behavior Scales (VABS), while ASD diagnosis was confirmed by ADOS and ADI-R. Mean scores on the hyperactivity subscale of the ABC were compared by diagnostic group. We also separated the hyperactivity subscale into 2 subdomains: hyperactivity/impulsivity (10 of 13 subscale items), and inattention (3 of 13 subscale items), and compared these subdomain scores by diagnostic group. We calculated Pearson correlation coefficients for the subscale and subdomain scores vs. SCQ, MSEL, and VABS scores. Associations between scores and demographic (income, parental age, education, and race) or environmental factors (distance from major road as a measure of air pollution, prenatal vitamin use, maternal pre-pregnancy obesity) were assessed by t-tests. Linear regression was used to examine these associations adjusted for potentially confounding factors.

Results:

560 ASD cases, 391 TD controls, and 168 DD controls were included in these analyses. Mean

hyperactivity subscale scores increased from TD to DD, and from DD to ASD, with significantly higher scores in the ASD group compared to each of the other groups. 35% of ASD cases scored in the top quintile of hyperactivity/impulsivity subdomain scores, compared to 24% of DD and 2% of TD. 40% of the ASD group were in the top quintile of inattention scores, compared to 20% of the DD group and 1% of the TD group. Hyperactivity and inattention subdomain scores were highly correlated with ABC irritability, lethargy, and stereotypy subscales across diagnostic groups ($r \sim .5-.7$). Overall, scores were not correlated with VABS or MSEL scores, though hyperactivity subscale scores were moderately correlated with reduced MSEL expressive language scores in cases only ($r = .31$). In adjusted analyses, low maternal education (high school or less) was significantly associated with higher hyperactivity subscale and hyperactivity/impulsivity subdomain scores in case children (corresponding to ~ 4 point score increase), while maternal obesity was associated with lower hyperactivity scores (~ 3 point decrease). No other factors demonstrated associations with these scores.

Conclusions:

Our results demonstrate a high prevalence of hyperactivity/impulsivity and inattention problems in children with ASD, and suggest the need for further study of these issues in association with subphenotypes and risk factors in autism.

161.083 83 Internalizing Problems in Children with ASD. J. A. de Ruiter^{*1}, M. de Bruine¹, L. B. Pouw¹, E. Broekhof¹, L. Stockmann², K. Gadow³ and C. Rieffe¹, (1)*Leiden University*, (2)*Centrum Autisme Rivierduinen*, (3)*State University of New York*

Background: Over the last couple of years, cross-sectional studies have demonstrated that Autism Spectrum Disorders (ASD) are associated with internalizing problems. This is strongly linked to certain aspects of emotion regulation, such as coping strategies, and impaired social skills and negative experiences with peers.

Objectives: The aim of this study is to examine the extent to which aspects of emotion regulation and social functioning are related to symptoms of depression in children with ASD. Since a cross-sectional study is limited in addressing the pathways or processes that lead to these

symptoms of depression, longitudinal analyses will also be conducted which might discover causal relationships.

Methods: The study included 120 high functioning boys (63 with ASD, 57 TD, mean age 139 months), who filled out self-report questionnaires on depression, coping strategies (problem solving, seeking social support, externalizing, internalizing, distraction, and trivializing) and social functioning (victimization and negative friendships).

Results: Maladaptive coping positively predicted symptoms of depression in boys with ASD. Independently of coping strategies, victimization and negative friendship interactions also positively predicted symptoms of depression.

Conclusions: This study shows that boys with ASD who use avoidant and maladaptive coping strategies, experienced higher levels of depression. Furthermore, being bullied or having low quality friendships also uniquely contributes to symptoms of depression in boys with ASD. By conducting longitudinal analyses, it might be possible to identify with certainty factors that contribute to the development of depression. This is helpful since it could lead to indicating potential targets for intervention with the possibility of preventing later-onset mental health concerns.

161.084 84 Intolerance of Uncertainty and Coping Strategies As Correlates of Anxiety in Mothers of Children with ASD. M. Uljarevic¹, J. Lidstone², S. R. Leekam³, A. S. Le Couteur⁴, D. W. Evans⁵, M. H. Freeston⁴, H. McConachie⁴, J. Rodgers⁶ and M. Prior⁷, (1)*Wales Autism Research Centre, School of Psychology, Cardiff University, Cardiff, United Kingdom*, (2)*Cardiff University*, (3)*School of Psychology, Cardiff University*, (4)*Newcastle University*, (5)*Bucknell University*, (6)*School of Medical Sciences, Newcastle University*, (7)*Melbourne School of Psychological Sciences*

Background: Research indicates that mothers of children with ASD have higher risk of anxiety than both mothers of typically developing children and parents of children with other disabilities. Research to date has tended to focus on the burden of caring for an autistic child as the main factor underlying the development of anxiety in their mothers. Another less explored factor is coping style of parent: while some coping strategies (problem focused coping styles) can serve as a protective factor and a barrier to the

development of anxiety, other types of coping (emotion focused coping) serve as a risk factor for the development of anxiety. 'Intolerance of uncertainty' (IU) is currently considered to play a central role in the development and maintenance of anxiety disorders in the general population (McEvoy & Mahoney, 2011). IU is most commonly defined as a predisposition to react negatively to an uncertain event or situation, independent of its probability of occurrence and of its associated consequences (Buhr & Dugas, 2009). In general population, it has been shown that elevated levels of intolerance of uncertainty provoke hypervigilant reactions when individuals are faced with uncertain situations. Anxiety would then result from the constant shifting from a state of hypervigilance (linked to the uncertainty of the situation) to a state of avoidance (Gentes & Ruscio, 2011). Surprisingly, intolerance of uncertainty has not been considered as a risk factor for the development of anxiety in parents of children with ASD.

Objectives: To explore the likelihood of high levels of anxiety in mothers of children with ASD and the influence of mothers' coping style and intolerance of uncertainty.

Methods: To date, 37 mothers of children with ASD (mean age of children= 10.9 years, SD= 4) completed the Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith, 1983), the Ways of Coping Scae (WCS; Folkman et al., 1986) and the Intolerance of Uncertainty Scale (IOU; Freeston et al., 1994).

Results: 42% of mothers met the cut-off criterion for clinically significant anxiety. MANOVA was performed in order to examine whether there was a difference between potentially clinically anxious mothers and non-anxious mothers in terms of their IOU total scores and their use of problem- and emotion-focused coping strategies. There was a significant difference on the combined dependent variables (IOU total scores, problem-focused and emotion focused coping) ($p = .003$). When the results for the dependent variables were considered separately, it was shown that mothers who had elevated levels of anxiety had significantly higher intolerance of uncertainty scores ($p = .003$) and used emotion-focused style of coping ($p = .005$) significantly

more than mothers who did not have elevated levels of anxiety.

Conclusions: Our findings suggest that a systematic study of factors that lead to the development of anxiety in mothers is needed in order to arrive at a more complete conceptualization of this problem.

161.085 85 Mental Health Outcomes Amongst Higher Ability Adults with Autism and Adult Siblings of People with Autism. P. Moss*¹ and P. Howlin², (1)*University College London*, (2)*Institute of Psychiatry, King's College London*

Background: There is a lack of systematic research into the mental health of higher ability adults with a childhood diagnosis of autism who are in mid- to late-adulthood. Although reviews of clinical studies indicate that rates of mental health difficulties from childhood onwards are greater than in the general population, data on the prevalence of such difficulties, or the factors associated with them are inconsistent. Additionally, very little is known about the mental health of siblings of adults with autism spectrum disorders (ASD) thought to be 'unaffected' by ASD and its broader phenotype.

Objectives: (i) To explore the mental health difficulties experienced by higher ability adults with autism in mid- to late-adulthood and to consider what factors affect the rates of such difficulties; (ii) To examine the rates of mental health difficulties experienced by 'unaffected' siblings of individuals with ASD in adulthood.

Methods: Standardised measures were used to establish rates of mental health difficulties in 60 adults with autism who had all been assessed as having a normal non-verbal IQ (PIQ>70) when diagnosed in childhood (current average age = 44 years, range = 29 - 64 years). The same measures were used with 69 siblings of an adult brother or sister with autism (average age of = 40 years, range = 21 - 57 years). A range of cognitive and social assessments was used to examine the factors associated with rates of mental health difficulties in these two groups.

Results: The majority of the adults with autism did not have significant mental health difficulties and only 20% were rated as having 'poor' or 'very poor' mental health outcomes. In contrast,

'unaffected' adult siblings of individuals with ASD reported high rates of mental health difficulties. In both groups, depression and anxiety were the most commonly reported difficulties. Gender was significantly associated with rates of difficulties amongst siblings, with females more likely to experience mental health difficulties than males. However, no other specific factors were associated with rates of mental health difficulties in adulthood in either group.

Conclusions: This study is the first systematic investigation into the prevalence of mental health difficulties amongst adults with a childhood diagnosis of autism and a childhood non-verbal IQ in the normal range. Whilst rates of mental health difficulties in this sample were lower than expected, they were still higher than in the general population. The findings have significant service implications; there is a need to develop specialist mental health services for this population and / or for clinicians in general adult mental health services to be appropriately educated on how to engage with this population and recognise their unique presentations in relation to mental health difficulties. The high rates of mental health difficulties amongst 'unaffected' siblings, particularly females, of individuals with ASD are particularly pertinent given their potential care-giving role with regard to their adult sibling with ASD.

161.086 86 Mental Health Problems Among Siblings of Children with Autism. J. L. Taylor*, *Vanderbilt Kennedy Center*

Background:

As rates of autism spectrum disorder (ASD) diagnoses have risen dramatically over the past 40 years, so has the number of siblings growing up with a brother or sister with ASD. Despite the recent increase in research on siblings of individuals with ASD, there is no consensus on whether these siblings are at risk for negative outcomes. Some studies show that siblings exhibit more internalizing and externalizing problems, peer and conduct problems, hyperactivity, delinquent behavior, and withdrawal when compared to siblings of children without ASD. Others, however, report that siblings of individuals with ASD are well-adjusted and show no more negative outcomes than control groups. The present study examined patterns and predictors of one negative outcome that may be

especially prevalent among siblings of children with ASD – anxiety.

Objectives:

This study had two objectives: 1) Do siblings of children with ASD have higher rates of anxiety problems relative to a normed sample? and 2) Do characteristics of the parents and of the brother/sister with ASD predict sibling anxiety?

Methods:

Participants were 1755 siblings of children diagnosed with ASD, who were part of the Simons Simplex Collection. The siblings ranged in age from 3 – 18 years, with a mean of 9 years. Sibling anxiety was measured using the anxiety subscale of the Child Behavior Checklist. Independent variables included measures of behavior problems, IQ, and autism severity of the child with ASD, as well as parental history of psychiatric disorders and parental broader autism phenotype characteristics (collected from both mothers and fathers).

Results:

As a whole, siblings did not experience higher rates of borderline or clinical anxiety symptoms; 8% of siblings fell above the borderline range compared to 7% in the general population. Stratification of the sample by gender and age, however, revealed interesting findings. Although none of the age/gender groups had elevations in anxiety that reached the clinical range, male siblings in middle childhood were twice as likely as would be expected to fall above the borderline cutoff (13.3% of male siblings aged 6-11, compared to 7% in the general population). Higher levels of sibling anxiety were predicted by maternal and paternal history of anxiety disorders ($B_s = .46$ for maternal and $.36$ for paternal, $p_s < .01$), higher maternal pragmatic language ($B = .38$, $p < .001$), and more behavior problems in the child with ASD ($B = .03$ for internalizing problems and $.02$ for externalizing problems, $p_s < .001$).

Conclusions:

While siblings overall did not show elevated anxiety symptoms, higher rates of sub-clinical

anxiety problems among males and siblings in middle childhood are cause for concern. Discussion will focus on why these siblings might be at higher risk, and will place these findings in the context of the current literature.

161.087 87 Neural Response During Emotion Elicitation in ASD:

Importance of Depression History and Positive Emotion. C. A. Mazefsky^{*1}, T. Goldstein¹, T. N. Day², N. J. Minshew³ and G. J. Siegle³, (1)University of Pittsburgh School of Medicine, (2)University of Pittsburgh ACE, (3)University of Pittsburgh

Background: Research on emotional processes in ASD has primarily focused on emotion perception (rather than the experience of emotion) with emotional faces as stimuli. However, broad measures of emotion recognition do not differentiate adolescents with ASD with and without severe mood dysregulation (Siminoff et al., 2012), and it is unclear if neural activation to emotional faces would correspond to the problems observed when individuals with ASD experience more salient emotions. Given accounts of problematic emotional control and variability in emotional functioning within ASD, studies utilizing paradigms that directly manipulate emotional experiences and consider heterogeneity within ASD are needed.

Objectives: 1) Characterize reactivity in emotion regulation-related brain regions using a new task designed to elicit positive and negative emotion; 2) Investigate factors related to heterogeneity in emotional reactivity within ASD, including comorbid psychiatric diagnoses and continuous measures of the participants' typical emotional/behavioral functioning.

Methods: Participants to date include 21 adolescents aged 12-19 years old with ADOS/ADI-R-verified ASD and 19 TD controls without ASD or a psychiatric disorder. All participants had IQs above 80 and the groups did not differ in FSIQ or age, $p > .05$. Psychiatric diagnoses for the ASD group were established with the Autism Comorbidity Interview, with nearly half ($n = 10$) meeting criteria for past or current depression. All parents/participants also completed a battery of emotional/behavioral questionnaires. A 3T Siemens trio scanner, TR = 1.67, and P to A EPI acquisition were utilized for fMRI. In the scanner, participants completed a new affective continuous performance task that alternates between a modified continuous performance task and a coin

toss task (s/he calls the flip of a coin). Present analyses focused on six blocks of coin-flip tasks in which s/he: 1) wins money (positive affective induction), and 2) loses money (negative affective induction) impacting actual participant payments (up to \$30). Preliminary analyses focused on the amygdala (additional participants, brain regions, and questionnaires will be included in updated analyses).

Results: History of depression and differential responses to positive emotion emerged as important factors related to heterogeneity in amygdala reactivity in ASD. Mixed effects analyses for baseline-corrected percent change in right and left amygdala activity supported significant main effects of valence (win or lose trial) and diagnosis (TD; ASD+depression; ASD without depression), and a diagnosis by valence interaction, $p < .001$. Interestingly, the strongest effect was for positive emotion, with increased amygdala activity in the ASD without depression group and decreased amygdala activity for the ASD+depression group during win trials.

Conclusions: The findings highlight the importance of addressing within group variability in studies of emotional reactivity in ASD given *opposite* patterns of amygdala activity between participants with versus without a lifetime history of a depressive disorder. Implications for models of emotion dysregulation in ASD will be discussed, including the role of episodic mood disorders within the broader context of temperament and possible disruptions in the intensity and modulation of both positive and negative affect.

161.088 88 Neurophysiological Responses to Emotional Faces Discriminate Children with ASD and/or ADHD. C. Tye^{*1}, M. Battaglia², E. Bertolotti³, K. L. Ashwood¹, B. Azadi¹, P. Asherson¹, P. F. Bolton¹ and G. McLoughlin¹, (1)*Institute of Psychiatry, King's College London*, (2)*Laval University and Institut Universitaire en Santé Mentale de Québec*, (3)*Vita-Salute San Raffaele University*

Background: Children with autism spectrum disorder (ASD) demonstrate characteristic deficits in processing facial information, particularly emotional expressions. There are high rates of clinical and behavioural overlap between ASD and attention deficit hyperactivity disorder (ADHD), and emotional impairment is also shown in ADHD. Pure and comorbid cases, however, have not been directly compared using event-related potentials

(ERPs) that are able to measure distinct temporal stages in emotional processing.

Objectives: (1) To investigate the specificity of emotion processing abnormalities to ASD and ADHD and (2) to elucidate the neural basis of the common comorbidity between these two disorders.

Methods: The N170 (an index of structural encoding) and N400 (an index of contextual processing) ERP components were measured during passive presentation of face stimuli with different emotional expressions (neutral, anger, fear, disgust, joy) to groups of ASD (n=19), ADHD (n=18), comorbid ASD+ADHD (n=29) and typically developing (TD) controls (n=26).

Results: Subjects with ASD (ASD and ASD+ADHD) displayed reduced N170 amplitude across all stimuli, and reduced N170 amplitude for fearful versus neutral facial expressions, compared to children without ASD. Conversely, subjects with ADHD (ADHD and ASD+ADHD) demonstrated reduced modulation of N400 amplitude by fearful expressions at parietal sites and happy facial expressions at central sites, compared to subjects without ADHD.

Conclusions: These findings indicate that while children with ASD demonstrate deficits at structural encoding stages of face processing (indexed by the N170), children with ADHD show impairments in contextual processing of emotion (indexed by the N400), which suggests a dissociation between disorders on the basis of distinct temporal stages of emotion processing. The comorbid ASD+ADHD group display the unique deficits of both disorders in early and late emotion processing, supporting the comorbid disorder as an additive condition rather than a separate disorder with distinct impairments. This supports the use of objective neural measurement of emotional function to delineate pathophysiological mechanisms and guide clinical assessment.

161.089 89 Predictors of Co-Morbid Psychopathology in High-Functioning Children and Adolescents with Autism Spectrum Disorders. E. Bal^{*1}, B. E. Yerys², C. Luong-Tran¹, I. Eisenberg³, A. C. Sharber¹, B. Robustelli³, L. Kenworthy¹ and G. L. Wallace³, (1)*Children's National Medical Center*,

(2)Children's Hospital of Philadelphia, (3)National Institute of Mental Health

Background: Symptoms of internalizing (e.g., anxiety, and depression) and externalizing (e.g., Oppositional Defiant Disorder [ODD], Conduct Disorder [CD]) disorders are commonly seen in children and adolescents with Autism Spectrum Disorders (ASD) (Gadow et al., 2008; Simonoff et al., 2012; Weisbrot et al., 2005). However, predictors of these co-occurring conditions have received limited attention. In the broader literature, high levels of callous-unemotional (C-U) traits are consistently related to conduct problems (Essau et al., 2006). Moreover, strong associations between ADHD and internalizing and externalizing disorders are also documented (Barkley et al., 1990; Hartung et al., 2002; Pardini & Fite, 2010). Given these high rates of co-morbidity, identifying unique predictors of common co-occurring psychiatric symptoms in youth with ASD becomes a vital question.

Objectives: The purpose of the current study is to assess how well ADHD symptomatology and C-U traits concurrently and uniquely predict internalizing and externalizing symptoms within a well-characterized sample of youth with high functioning ASD. We hypothesize that ADHD symptoms will significantly predict internalizing symptoms (for generalized anxiety disorder [GAD] and dysthymia) and that C-U traits will significantly predict externalizing symptoms (for ODD and CD) in youth with ASD.

Methods: Ninety-five children, adolescents, and young adults with high functioning ASD (FSIQ: $M=109.06$, $SD=17.77$) ages 6-28 years ($M=13.36$, $SD=4.63$) participated in the study. ADHD, internalizing, and externalizing symptomatology were assessed via parent report using the Child and Adolescent Symptom Inventory-4R (CASI) or the Adult Inventory-4 (AI). C-U trait ratings were also provided by parents using the Inventory of Callous-Unemotional (ICU) traits. Hierarchical linear regression analyses were run to examine how well age, full-scale IQ, C-U trait ratings, and ADHD ratings sequentially predicted GAD, dysthymia, CD, and ODD symptoms.

Results: Regression analyses revealed that ADHD symptoms were a significant predictor of

GAD symptoms, explaining 26% of the variance ($p<.001$). Age also predicted GAD symptoms, though it explained only 1% of the variance ($p<.01$). Age and ADHD significantly predicted dysthymia symptoms; age explained 21% of the variance and ADHD explained an additional 8% of the variance ($ps<.001$). As expected, C-U traits significantly and uniquely predicted CD symptoms, explaining 21% of the variance ($p<.001$). Both C-U traits and ADHD significantly predicted ODD symptoms; C-U traits explained 15% of the variance, and ADHD explained an additional 11% of the variance ($ps<.01$). Full-scale IQ was not a significant predictor of internalizing or externalizing symptoms.

Conclusions: The present study showed that ADHD significantly predicted GAD, dysthymia, and ODD symptoms whereas C-U traits significantly predicted CD and ODD symptoms in youth with ASD. Age was also a significant positive predictor of primarily dysthymia symptoms. Collectively, the results indicate that the degree of ADHD symptoms and C-U traits in ASD impacts the severity of internalizing and externalizing symptoms, respectively. These findings highlight the importance of assessing comorbid psychopathology in children with ASD to identify potential risk factors and to develop more effective treatment plans.

161.090 90 Sexual Behavior in Adolescents and Young Adults Diagnosed with Autism Spectrum Disorder: A Parent's Perspective. M. J. Lang*, D. R. Morrison, L. Martin and K. Shier, *Azusa Pacific University*

Background: Adolescence is a time where sexuality emerges, and individuals with autism spectrum disorder (ASD) experience the same bodily changes as typically developing peers. ASD is characterized by deficits in social interactions and communication, as well as the presence of restricted and stereotypic patterns of behavior. Due to the deficits in social interactions individuals with ASD may have a difficult time expressing themselves appropriately. Past research has shown that individuals with autism display inappropriate sexual behaviors. However, these studies have had limited sample size and diversity. Further research is necessary to provide a larger and more diverse sample size in order to determine the extent of the problem and to develop effective behavioral and educational strategies to prevent problem behaviors.

Objectives: Our goal was to determine the extent of inappropriate sexual behaviors in adolescents with autism across a broad sampling of the U.S. population. Special attention was given to differences in sexual behavior between individuals diagnosed with AS, mild-to-moderate, and moderate-to-severe autism. This study will increase understanding of sexuality in ASD and shed light on the need for interventions to assist individuals with ASD in coping with their behavioral urges.

Methods: The researchers utilized the Sexual Behavior Scale (SBS) developed by Stokes and Kaur (2005) to examine the behavior of individuals with ASD between the ages of 8 and 25. This measure identifies parents' attitudes and perceptions of their child, adolescent, and/or young adult's behavior across five domains: 1) social behavior; 2) privacy awareness; 3) sex education; 4) sexual behavior; and 5) parental concerns. Participants were recruited through the Interactive Autism Network (IAN), which is intended for families, professionals, and researchers to share information. A link to the SBS, which was on Survey Monkey, was provided to families who were members of IAN. There were 232 parent/caregiver participants answering in reference to their children with ASD. It was hypothesized that parents/caregivers would report inappropriate sexual behaviors and that differences would be expressed across severity of diagnosis, age, gender, region, and ethnicity.

Results: The parental perspective came predominantly from biological mothers (87.9%). While the majority of respondents were caucasian (77.2%), the sizable sample enabled insight into parental concerns across diverse ethnic backgrounds. A sizable percentage, 45.7%, indicated that their child had touched private body parts in public. There was also a significant negative correlation between age of the individual and touching private body parts in public ($r = -.178$; $p = 0.01$). Qualitative results indicated significant concern in regards to social behavior and social acceptance. Several parents also expressed their gratitude that this issue is being studied indicating the need for more research in this area.

Conclusions: These findings will provide an understanding of the need for privacy, appropriate

sex education, and social skills training in adolescents and young adults with ASD. While our analysis is ongoing, we hope that these findings will assist in the development of behavioral and educational strategies that will facilitate healthy and appropriate sexual and social behavior for individuals with ASD.

161.091 91 Significant Gender X Autism Status Interactions in Middle Childhood On Variables Related to Difficult Temperament. B. D. Barger¹, J. M. Campbell*² and C. A. Simmons¹, (1)University of Georgia, (2)University of Kentucky

Background: Temperament is an understudied construct in the autism literature and in the handful studies to date few researchers have investigated gender differences. Furthermore, in the childhood temperament literature most researchers have relied on instruments designed to measure either Thomas and Chess or Rothbart's conceptualizations of temperament.

Objectives: This study seeks to determine whether temperament variables measured with the new Inventory of Children's Individual Differences-Short Form (ICID; Deal, Halverson, Martin, Victor, & Baker, 2005) differentiate children with ASD from typical children, as well as determine whether there are any significant ASD status X gender interactions on temperament variables in middle childhood.

Methods: Here we report a 2 (ASD versus typical)* X 2 (Gender) age controlled MANCOVA comparing 113 ASD (93 male; 20 female) and 372 control children (163 male; 209 female) between the ages of 8 and 12 (Middle Childhood; MC). Data from ASD children was collected on-line via the Interactive Autism Network and data from typical children was taken from the norming sample data set.

Results: Pillai's Trace statistics indicated significant ASD X gender interactions [$F(1, 15) = 2.032$, $p < .05$], significant gender differences [$F(1, 15) = 1.321$, $p < .05$], and significant differences between ASD and typical children: [$F(15, 1) = 39.574$, $p < .001$]. Follow up Wesch's F tests indicated significant gender X diagnostic status interactions for antagonism [$F(1, 426) = 5.06$, $p < .05$], consideration [$F(1, 426) = 4.02$, $p < .05$], intelligence [$F(1, 426) = 4.04$, $p < .05$], negative emotion (anger) [$F(1, 426) = 12.81$, $p < .05$].

.05], and strong willed [$F(1, 426) = 4.27, p < .05$]. Diagnostic group differences were found with ASD children scoring lower on achievement [$F(1, 426) = 118.21, p < .001$], compliance [$F(1, 426) = 151.18, p < .001$], consideration [$F(1, 426) = 227.39, p < .001$], intelligence [$F(1, 426) = 43.12, p < .001$], openness [$F(1, 142.54) = 203.57, p < .001$], positive emotion [$F(1, 426) = 66.30, p < .001$], and sociability [$F(1, 426) = 355.95, p < .001$] and higher on antagonism [$F(1, 426) = 44.08, p < .001$], distractible [$F(1, 426) = 15.59, p < .001$], fear/insecure [$F(1, 426) = 44.50, p < .001$], negative emotion (anger) [$F(1, 426) = 92.20, p < .001$], shy [$F(1, 426) = 259.24, p < .001$], and strong willed [$F(1, 426) = 61.88, p < .001$]. No group differences were found for activity level [$F(1, 426) = 1.71, p = .192$] or organized [$F(1, 426) = 3.03, p = .082$].

Conclusions: These results indicate that in MC females with ASD are perceived by their parents as having more difficult temperaments and as being less intellectually capable than boys with ASD. Furthermore, there were widespread temperament differences between children with ASD and typical children with largest differences found on sociability and shyness. Future research may seek to determine whether the sources of the gender X diagnostic status interactions are due to true behavioral differences using more objective methods.

*This project is funded by a grant from the Organization for Autism Research

161.092 92 Sleep Quality and Parent-Adolescent Relationships. M. M. Abdullah* and W. A. Goldberg, *University of California, Irvine*

Background: Pediatric sleep debt, with a recent estimate prevalence of 45% for mild sleep disturbances in a typically developing sample, ranks as a public health problem of concern (Souders et al., 2009). Even high prevalence rates characterize children with autism spectrum disorders (ASD); recent estimates of at least moderately severe sleep problems among children with ASD have reached 66% (Souders et al., 2009). Symptoms of poor sleep quality among children with ASD have included difficulty falling asleep, restlessness during sleep, frequent night-waking, and early waking (Mayes & Calhoun, 2009). Children with ASD with problematic sleep demonstrate greater communication impairment

as well as aggression and hyperactivity compared to children with ASD without problematic sleep (Goldman et al., 2011). Links between sleep quality and social relationships in the context of ASD demand empirical investigation.

Objectives: To examine the associations between the quality of sleep of adolescents with ASD and the quality of family relationships.

Methods: Participants were 31 adolescents who had been clinically diagnosed with ASD and their married mothers and fathers. Adolescents' age ranged from 12-18 years. Full-scale IQ scores averaged 95.48 ($SD = 18.63$). There were more adolescent boys (90%) compared to adolescent girls in the sample. Data collection took place in family homes; adolescents and parents completed questionnaires. Sleep quality was measured using two questionnaires: (1) the Children's Sleep Habits Questionnaire (CSHQ; Owens et al., 2000) is a parent-report measure designed to assess sleep functioning in children; (2) the School Sleep Habits Survey (SSHS; Wolfson & Carskadon, 1998) is an adolescent self-report, which asks about typical sleeping and waking behaviors. Quality of family relationships was measured using the Network of Relationships Inventory-Relationship Qualities Version (NRI-RQV; Buhrmester & Furman, 2008), which is an adolescent and parent measure assessing supportive and discordant parent-adolescent relationship quality. ASD symptoms were measured using the Social Communication Questionnaire (SCQ; Rutter, Bailey, & Lord, 2003), a brief parent-report instrument.

Results: When controlling for symptoms of ASD, parental reports of poorer adolescent sleep quality were significantly related to adolescent reports of less mother-adolescent closeness ($r = -.404, p = .027$) and marginally less father-adolescent closeness ($r = -.332, p = .073$). When controlling for symptoms of ASD, adolescent reports of greater daytime sleepiness were related to greater maternal reports of mother-adolescent discord ($r = .456, p = .015$) and marginally greater paternal reports of father-adolescent discord ($r = .360, p = .060$).

Conclusions: Parents of children with ASD report adolescent sleep issues as a major concern (Guinchat et al., 2012). Results from the current

study, while not addressing temporal ordering, confirm that parents and adolescents with ASD perceive less closeness and more discord in their relationships when adolescents with ASD have sleep disturbances and daytime sleepiness. The findings from the current study have clinical implications for understanding physiological correlates of impaired fundamental social relationships—mother-adolescent and father-adolescent relationships.

161.093 93 Suicidal Behaviour in Adolescents with Autism Spectrum Disorders. T. Hurtig^{*1}, I. K. Moilanen¹, M. L. Mattila¹, S. Kuusikko-Gauffin¹, K. Jussila¹ and H. Ebeling², (1)*University of Oulu*, (2)*University and University Hospital of Oulu*

Background:

Individuals with Autism Spectrum Disorders (ASDs) often suffer from clinical anxiety or depressive symptoms in which suicidal behaviour is a common feature. In addition, aggression and impulsivity may relate to ASDs as well as to suicidal behaviour. However, suicidal behaviour in individuals with ASDs is little studied.

Objectives:

Our aim was to study suicidal behaviour in adolescents with ASDs compared to typically developed adolescents.

Methods:

The ASD sample included 76 adolescents (age range 8-24 years, mean age 12,8 years, 56 boys, 17 girls), most of whom were recruited from child psychiatric outpatient clinic of University Hospital of Oulu, Finland. Some of them were recruited from the epidemiological study of Asperger syndrome in the catchment area of the hospital. All went through rigorous diagnostic examination for ASDs including e.g. ADI-R and ADOS. The control group included 76 typically developed adolescents (age range 8-16 years, mean age 12,3 years, 35 boys, 40 girls) recruited from mainstream schools in the city of Oulu, Finland. They were screened with the ASSQ and excluded if the total score was 7 or more. All participants (n=152) and their parents were interviewed with a semi-structured Kiddie-SADS-PL psychiatric interview in the year 2005, 2006, 2007 or 2008 as a part of a larger study of ASDs. Kiddie-SADS-PL

includes the following items measuring suicidal behaviour: thoughts of death, suicidal ideation, suicide attempts, and deliberate self-harm (e.g. cutting and burning one-self). Lifetime suicidal behaviour in the study groups was analysed using the chi square testing.

Results: Adolescents with ASDs presented more thoughts of death (34.2% vs. 13.2%, p .002) and suicidal ideation (18.4% vs. 3.9%, p .008) than typically developed adolescents. There were negligible differences in suicide attempts (1.3% vs. 0%, NS) and deliberate self-harm (5.3% vs. 2.6%, NS) between adolescents with ASDs and typically developed adolescents. Age and gender did not have any effect on the results.

Conclusions:

Children and adolescents with ASDs may have suicidal thoughts. This should be kept in mind when examining psychosocial well-being of these individuals in order to prevent negative outcomes and reduced mental health among individuals with ASDs.

161.094 94 Symptoms of Psychiatric Comorbidity and Social Functioning in Adolescents with ASD. C. E. Lin^{*1}, M. N. Park², S. Bates³, J. Hopkins⁴ and E. Laugeson¹, (1)*UCLA Semel Institute for Neuroscience & Human Behavior*, (2)*UCLA Semel Institute for Neuroscience and Human Behavior*, (3)*UCLA PEERS Program*, (4)*UCLA PEERS Clinic*

Background:

Youth with autism spectrum disorders (ASD) frequently present with psychiatric comorbidities that can exacerbate existing social challenges, such as increased feelings of loneliness, dissatisfactory interpersonal relationships, and decreased social competence. Examining the relationship between psychiatric comorbidities and the social functioning of adolescents with ASD may guide the development of effective interventions.

Objectives:

Investigate the relationship between symptoms of psychiatric disorders and social functioning in adolescents with ASD.

Methods:

Data were collected from an outpatient clinic sample of 76 adolescents with ASD (12-18 years old) and their parents referred for a parent-assisted social skills treatment. Baseline symptoms of attention-deficit/hyperactivity disorder (ADHD), depression, and social anxiety disorder (SAD) were obtained from parent- and adolescent self-report measures. ADHD symptoms were measured using the Swanson, Nolan, and Pelham-IV (SNAP-IV; parent-report), SAD from the Social Anxiety Scale-Adolescents (SAS-P; parent-report) and the Social Anxiety Scale-Adolescents (SAS-A; self-report), and depression based on the Children's Depression Inventory (CDI; self-report). Social functioning was assessed using the Social Responsiveness Scale (SRS; parent-report), Social Skills Improvement System-Parent (SSIS-P), and Friendship Qualities Scale (FQS; self-report). Correlations between baseline psychiatric symptoms and social functioning were examined.

Results:

Overall, symptoms of ADHD, SAD, and depression were associated with poorer social functioning. Inattention was related to impairments in overall social functioning [$r(66) = .332, p < .01$], such as social awareness [$r(66) = .365, p < .01$], social cognition [$r(67) = .299, p < .05$], more pronounced autistic mannerisms [$r(66) = .324, p < .01$], and responsibility skills [$r(40) = -.384, p < .05$]. Hyperactivity/impulsivity and oppositionality were associated with similar challenges, including impaired social awareness [$r(66) = .396, p < .01$]. Inattention was related to better companionship quality [$r(69) = .248, p < .05$].

Social anxiety was related to impairments in social functioning and some prosocial behaviors. Higher parent-reported social avoidance/distress to new situations/unfamiliar peers was related to greater overall social difficulties [$r(68) = .373, p < .05$]. Social avoidance/distress generally experienced with peers was associated with poorer companionship quality [$r(67) = -.241, p < .05$], overall social impairment [$r(68) = .474, p < .01$], and engagement skills [$r(40) = -.397, p < .05$]. Alternatively, greater symptoms were linked with better cooperation [$r(40) = .481, p < .05$] and responsibility skills [$r(40) = .362, p < .05$]. Adolescent-report of SAD indicated similar

findings of less satisfactory friendship quality and poorer social skills, but greater social awareness [$r(68) = -.315, p < .05$].

Depressive symptoms were associated with less satisfactory friendship quality. Higher ratings were related to decreased self-reported companionship quality [$r(67) = -.254, p < .05$], peer conflict [$r(68) = .255, p < .05$], and helpfulness with friendships [$r(67) = -.259, p < .05$].

Conclusions:

Comorbid symptoms of ADHD, anxiety, and depression were correlated with impaired social functioning and poorer friendship quality. Some aspects of anxiety were related to positive social behaviors. Further research exploring the connection between co-occurring psychiatric symptoms and social functioning in ASD is needed.

161.095 95 The Neurocognitive and Psychiatric Profile of Callous Unemotional Traits in Autism Spectrum Disorders. V. Carter Leno*¹, T. Charman², C. Jones³, F. Happé⁴, G. Baird⁵, A. Pickles¹ and E. Simonoff⁴, (1)*Institute of Psychiatry*, (2)*Institute of Education*, (3)*University of Essex*, (4)*Institute of Psychiatry, King's College London*, (5)*Guy's Hospital*

Background:

Many individuals with Autism Spectrum Disorders (ASD) have been described to display a lack of empathy for others and lack of remorse for their actions. These behaviours are similar to those seen in individuals with Callous Unemotional (CU) traits. CU traits are found in a subgroup of individuals displaying anti-social behavior and these traits are associated with a severe and persistent pattern of anti-social behaviors. There has been debate about the prevalence and origins of CU traits among people with ASD.

Objectives:

To determine the prevalence of CU traits in adolescents with ASD and whether they display similar psychiatric and neurocognitive correlates to those found in typically developing populations

Methods:

This study involved 89 16 year old adolescents from the Special Needs and Autism Project (SNAP), a longitudinal, population-based cohort. Parent-reported symptoms of CU traits were measured using the Anti Social Processes Screening Device (APSD) and Conduct Problems Questionnaire (SDQ), for both measures, thresholds indicative of a significant problem were employed. Three groups were identified: those with CU and CP (CU+CP;n=8), those with only CU (CU-CP;n=38) and those with neither (ASD only; n=41). Independent measures included other psychiatric subscales, the Social Responsiveness Scales (SRS), IQ and performance on the Ekman emotion recognition task for six emotions: happiness, sadness, anger, fear, disgust and surprise.

Results:

Prevalence. 53% of the sample were above threshold for CU traits (above a t-score of 65), however within the CU+ group only 17% also displayed CP.

Psychiatric (SDQ). A multiple regression using group as a predictor variable and controlling for IQ found lower prosocial behaviour scores in the CU-CP and CU+CP groups compared to ASD only ($p<0.01$) but there were no group differences on the emotional and hyperactivity subscales.

IQ. The CU+CP displayed significantly lower verbal IQ ($p<0.05$) but not performance IQ than both the CU-CP and ASD only groups.

Emotion Recognition. There were no significant differences between scores on the Ekman emotional recognition task except in the Happiness category where the CU+CP group performed more poorly than both groups ($p<0.05$).

Relationship with autism severity and SRS Subscales. Autism severity was rated as higher in both groups displaying CU traits ($p<0.05$) but the relationship was not significant for clinician ratings of autistic symptoms or diagnosis. Subscales on the SRS relating to communication, awareness, cognition and motivation were all higher in both CU groups compared to ASD only

(all $p<0.01$). Multiple regression accounting for communication found no differences in the mannerisms subscale between groups.

Conclusions:

CU traits are common in adolescents with ASD, but only a minority have CP, in contrast to the correlates seen in non-ASD populations. Furthermore, the typical deficit in fear recognition associated with CU traits was not replicated in our ASD sample. Those with CU traits had lower verbal IQ, poorer parent-rated communication, awareness and motivation. The present findings support the idea that CU traits in people with ASD may have a different origin than those seen in typically developing people, although further research is required.

161.096 96 The Physiological Correlates of Anxiety in Autism Spectrum Disorders. M. J. Holllocks*¹, L. E. Grayson¹, A. Papadopoulos², P. Howlin¹ and E. Simonoff¹, (1)*Institute of Psychiatry, King's College London*, (2)*King's College London*

Background:

People with ASD are known to display increased levels of anxiety symptoms and disorders. However the physiological correlates of this vulnerability to symptoms of anxiety are yet to be fully explored.

Objectives:

To determine whether people with ASDs show a similar physiological response to psychosocial stress as measured by salivary cortisol and heart rate (HR) compared to controls, and whether physiological response relates to anxiety.

Methods:

This study includes 53 boys with ASDs and 23 typically developing controls all participants were male and their full-scale IQ was ≥ 70 . We specifically recruited ASD participants with and without anxiety problems.

Anxiety was assessed using the Spence Child Anxiety Scale (SCAS) – parent version. For the present analysis, the ASD group was collapsed and anxiety symptoms treated as an independent

measure. Participants underwent a psychosocial stress test consisting of 40 minutes rest, 20 minutes stress and finally 40 minutes recovery. The stress test comprised a non-verbal drawing task and a public speaking task. Six cortisol samples were taken, at baseline, and then at 20 minute intervals. HR was measured continuously and divided into five 20 minute segments.

Results:

The groups differed in age (ASD 12.8 years vs. controls 14 years ($p \leq .05$)) but not FSIQ (102 vs. 116), as expected by design, the ASD group had significantly higher anxiety ratings (mean SCAS-P; 33 vs. 9, $p \leq .01$).

Cortisol. A repeated measures ANOVA revealed significant main effects for group ($p = .02$), time ($p \leq .01$) and a group \times time interaction ($p = .03$). The cortisol concentration was significantly lower in the ASD group at each post-stress time-point (all $p \leq .01$).

Mean Heart Rate. A repeated measures ANOVA also revealed significant main effects of group ($p = .02$) and time ($p \leq .01$) and a significant group \times time interaction ($p = .011$). The ASD group mean HR was significantly higher in the resting phase and in the first 20 minutes of the recovery phase (both $p \leq .01$), but did not differ in the stress phase.

Stress responsiveness. The ASD group showed reduced stress responsiveness compared to controls as demonstrated by reduced cortisol (.54 versus 2.33 ($p = .011$)) and a less marked increase in HR 5.4 beats-per-minute versus 10.4 ($p \leq .01$)

A regression analysis to examine the independent roles of anxiety and participant group on physiological responsiveness revealed that increasing SCAS score ($p = .06$) but not group predicts a decreased cortisol response to social stress.

Analysis of HR responsiveness revealed a significant SCAS by group interaction ($p = .012$). In the control group, increasing SCAS scores were positively associated with increased stress reactivity while the opposite relationship was seen in the ASD group.

Conclusions:

Children with ASD displayed elevated resting HR and a lack of responsiveness in both HR and cortisol when entering a stressful situation. Furthermore the relationship between stress responsiveness and baseline anxiety symptoms appears to differ between groups. In those with ASD reduced physiological response to stress is associated with greater levels of anxiety. Results will be discussed in the context of heart rate variability.

161.097 97 The Relationship Between Parents' Mental Health and the Gravity of Autism Symptoms. S. B. Machado, M. P. Ponde*, M. I. Celestino and J. P. Serra, *BAHIANA School of Medicine and Public Health*

Background: Autism spectrum disorders are neurodevelopmental disorders that involve fundamental deficiencies in social and communication. This disorder can alter family dynamics as an important stressor for caregivers

Objectives: The present study is aimed at ascertaining whether alterations in the mental health of parents/caretakers of autistic children, particularly anxiety and depression, have a negative effect on the autistic symptoms in children. Furthermore, this work intends to verify which aspects are associated with the psychic illnesses of these caretakers.

Methods: This is an observational study with a transversal cut. The target population consisted of students of a specialized school for autistic children in the state of Bahia. The sample of this study was made up of 106 parents/children. The following tools have been used with parents: a socio-demographic data form; the Portuguese version of the HADS (Hospital Anxiety and Depression Scale) to assess the symptomatology of caretakers; and the Portuguese version of ABC (Aberrant Behavior Checklist) to assess the gravity of the symptoms in children. Parents have been dichotomized into two groups: SICK (when they presented, according to the total sum of points in the scale, indication of anxiety and/or depression) and NOT SICK (when the total sum of points in the scale was inferior to the cut-off point). Co-variables have been distributed according to the exposition variable (gravity of the symptoms in children) with the objective of

analyzing the differences among the group of caretakers.

Results: The sample has displayed a prevalence of women (89.4%) – given that the majority of the sample has been composed of the mothers of the autistic children. 33% out of the assessed caretakers have presented anxiety, 26.4% depression and 18% both disorders. Among the caretakers without AD (anxiety and/or depression), 10.8% had children with severe autistic symptoms, against 34.1% of the fathers without AD ($p=0.0009$). The prevalence of AD on mothers aged up to 30 has been of 57.1%, against 14.9% of the group aged between 30 and 45 and 31.8% of the group aged above 45 ($p=0.01$). The presence of another child has shown itself as a worsening factor for the health of parents thus increasing the prevalence of AD within this group from 28.6 to 50% ($p=0.008$).

Conclusions: This study has demonstrated a high prevalence of depression and/or anxiety in the assessed sample (40.5%). The comparison between the gravity of symptoms of children and the symptoms of parents has indicated that the prevalence of children with severe autistic symptoms has been of 10.8% in the group of parents with lower scores in the HADS and 34,1% in the group of parents with higher scores in the HADS, therefore evidencing a direct relationship between the gravity of children's symptoms and the worsening of parents' mental health. The low age range of mothers has worked as a predictor of maternal illnesses.

161.098 98 The Swedish Eating Assessment for Autism Spectrum Disorders (SWEAA) -Development and Validation of a Self-Report Questionnaire Targeting Disturbed Eating Behaviours within the Autism Spectrum. L. Karlsson*¹, M. Råstam² and E. Wentz¹, (1)*Gillberg Neuropsychiatry Centre, University of Gothenburg*, (2)*Child and Adolescent Psychiatry*

Background: The presence of eating and mealtime problems in autism spectrum disorders (ASD) is clinically acknowledged but rarely investigated in those with normal intelligence. Disturbed eating behaviour in ASD strongly influences everyday life of the individual but also contributes significantly to the caregiver burden. Examples of eating disturbances linked to ASD are selective eating, food neophobia, pica, rumination, overeating and polydipsia. Despite the clinical relevance, eating and mealtime problems have

been scarcely explored within the autism spectrum and prior research has mainly focused on individuals with a concurrent intellectual disability (i.e. mental retardation).

Objectives: The aim of the study was to develop and validate a web-based self-report questionnaire exploring disturbed eating in individuals with ASD and normal intelligence.

Methods: Based on literature review and clinical experience a questionnaire pertaining to eating and mealtime problems within the autism spectrum was developed. The questionnaire was completed by individuals with ASD and normal intelligence, 15-25 years old ($n=57$; male:38, female:19), and by healthy age-matched controls ($n=31$; male:15, female:16). The validation focused on basic psychometric properties of reliability and validity. Statistical analyses comparing the two groups were also performed as well as a four week interval test-retest.

Results: The instrument showed high levels of reliability, convergent and discriminant validity and scaling properties. Logistic regression analyses discerned areas of *Simultaneous capacity* and *Social situation at mealtime* as the best predictors of ASD. BMI did not differ between the ASD group and controls. Significant negative correlations were found between BMI and the subscales *Eating behaviour* and *Social situation at mealtime* in the ASD group, i.e. the more deviant eating behaviour the lower the BMI.

Conclusions: The present study suggests that SWEAA is a reliable and valid instrument for assessing eating and mealtime problems in ASD.

161.099 99 The Utility of the Spence Children's Anxiety Scale (SCAS) in Screening for Anxiety Disorders in Children and Youth with Autism Spectrum Disorders. I. Magiati*¹, J. W. Tan¹, H. B. Z. NUR¹, J. Y. Chan¹, K. Poon², M. Sung³ and D. Fung³, (1)*National University of Singapore*, (2)*National Institute of Education*, (3)*Institute of Mental Health*

Background: The experience of anxiety is often an associated feature of Autism Spectrum Disorders (ASD) and children and young people with ASD are at increased risk for comorbid anxiety disorders. As these difficulties can significantly exacerbate overall disability levels in the ASD population, there is a need accurately to

screen and identify individuals with clinical levels of anxiety in the community in order to enable them to receive appropriate assessment and intervention. However, as existing anxiety scales have been primarily developed for children and youth without ASD, it is important that the usefulness of these measures is evaluated in the ASD population

Objectives: This study will assess the utility of the Spence Children's Anxiety Scale (SCAS) as an accurate early indicator of significant anxiety difficulties and in screening for anxiety disorders in children and youths with ASD.

Methods: 30 caregivers of 6-17 year old children and young people with an established professional diagnosis of ASD completed the brief Parent Report version of the SCAS and also participated in an in-depth, follow-up clinical diagnostic interview for anxiety using the Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime version (K-SADS-PL). Inter-rater reliability for the administration and scoring of the K-SADS-PL was also established. Caregivers also completed the Developmental Behaviour Checklist (DBC) and the Scales of Independent Behaviour-Revised (SIB-R) in order to provide information on their child's adaptive functioning and on other behavioural or emotional difficulties.

Results: Data collection has been completed and data is currently being analyzed. The frequencies of children meeting full as well as subthreshold DSM-IV-TR anxiety criteria will be calculated. Specificity, sensitivity, reliability coefficients and positive and negative predictive values will be calculated for the SCAS total and subscale scores and compared to values reported from limited literature on the use of other non-ASD specific tools in screening for anxiety disorders in ASD. The utility of SCAS in higher and lower functioning children with ASD (defined as SIB-R standard scores > or < 70 respectively) is also examined.

Conclusions: Preliminary inspection of the results suggests that the SCAS Parent Report is likely to be a useful screening tool that can effectively identify children and youths with ASD with high anxiety symptomatology who may benefit from further assessment for a possible clinical diagnosis of anxiety disorders.

161.100 100 Understanding Comorbid Conditions in Children and Adolescents with ASD. E. Hanson*¹, S. Maisel², K. Porche² and C. Powell², (1)*Children's Hospital Boston*, (2)*Boston Children's Hospital*

Background:

Little previous research has been aimed at understanding the prevalence and changing nature of comorbid conditions in children with Autism Spectrum Disorders (ASD) as they age. Research suggests that there are high rates of comorbid conditions present (Bruin, Ferdinand, Meester, Nijs, & Verheij, 2006; Kim, Szatmari, Bryson, Streiner, & Wilson, 2000; Lainhart, 1999), however, sample sizes have been limited and the range of psychiatric comorbidities examined has been limited primarily to depression (Ghaziuddin, Ghaziuddin, & Greden, 2002), anxiety (Kim et al., 2000), or attention deficit/hyperactivity disorder (Gillberg & Billstedt, 2000). A comprehensive evaluation of several comorbid conditions, how they change with age and comparisons to typically developing groups has not been reported and there are few tools to assess these changes. Pandolfi, Magyar, and Dill (2012) reported an initial assessment of multiple symptoms using the Child Behavior Checklist 6-18 (CBCL) (Achenbach & Rescorla, 2000, 2001), which provided a preliminary account of co-morbid problems in older adolescents, but also suffered from many of the same issues as previous papers.

Objectives:

(1) Determine the overall prevalence of comorbid symptoms in children and adolescents with ASD and the overall amount of comorbidities, and (2) assess possible trends in comorbid conditions when comparing age and gender cohorts to see how these develop over time and assess prevalence of symptoms compared to age matched typically developing siblings.

Methods:

Subjects with ASD as well as typical siblings were recruited from the Simons Simplex Collection and the Boston Autism Consortium. All consenting participants received a comprehensive diagnostic assessment including an Autism Diagnostic Observation Schedule (ADOS), the Autism Diagnostic Interview-Revised (ADI-R), cognitive,

language, behavioral and adaptive skills assessments. To assess symptom presentation, the two forms of the Child Behavior Checklist were used (1.5-5 years of age and 6-18 years of age). There is overlap in several subscales that allow for direct age and gender cohort comparisons to determine how aging and gender affects these symptoms. The Syndrome subscales of interest were: aggression, attention, somatic, withdrawn/depressed and anxious/depressed symptom groups. Scores on these subscales were categorized into groups based on the clinical cutoff scores: below threshold, borderline, or above clinical cutoff.

Results:

To date, we have enrolled 2851 individuals (from 2842 families). Individuals with ASD ranged in age from 3 to 18 years, and had a mean IQ of 84.4 (SD = 26.3). The most common elevated (i.e. above clinical cutoff) subscales on the CBCL 6-18 were Thought Problems, Attention Problems and Withdrawn/Depressed; CBCL 2-5 common elevations were Withdrawn, Attention Problems and Emotionally Reactive with this trend continuing when controlling for IQ. Significant elevations were not different between males and females with the exception of the Attention subscale, on which males scored higher than females. Analysis of DSM scales, longitudinal data and comparisons to sibling control groups is ongoing.

Conclusions:

Co-morbid symptoms among individuals with ASD were extremely common, with 1867 (65.5%) participants surpassing the clinical cutoff on the syndrome scales of the CBCL. Analyses are ongoing for comparisons with typical siblings.

Treatment Trials: Behavioral Interventions Program 162 Treatments: Psychopharmacological, Biomedical, Complementary and Technologically Based Interventions

This session includes papers related to the following interventions: psychopharmacological, biomedical, complementary and technology mediated

162.101 101 A Randomized Controlled Trial of a Course of Oxytocin Nasal Spray to Treat Youth with Autism. A. J. Guastella*¹, S. L. Einfeld¹, K. M. Gray², N. Rinehart², B. J. Tonge², I. B.

Hickie¹, G. Alvares¹, C. Keating² and C. Cacciotti¹,
(1)University of Sydney, (2)Monash University

Background: A diagnostic hallmark of autism spectrum disorders is a qualitative impairment in social communication and interaction. Deficits in the ability to recognize the emotions of others are believed to contribute to this. There is currently no effective treatment for these problems. Recent advances in the field of social neuroscience suggest the hormone and neuropeptide oxytocin enhances social behavior across mammalian species. Research also suggests that the administration of oxytocin nasal spray improves theory of mind, trust and other aspects of social cognition in neurotypical humans and people diagnosed with autism.

Objectives: The aim of this study was to conduct a randomized controlled trial of oxytocin nasal spray to treat social impairments found in youth diagnosed with autism. We aimed to determine whether oxytocin nasal spray would improve social interaction, social cognition, and reduce repetitive behavior, in comparison to a placebo nasal spray.

Methods: This trial recruited 50 male participants aged between 12 and 18 who were diagnosed with autism. We assigned each of these individuals to receive either oxytocin (18 or 24 IU) or an identically matched placebo, twice per day over an eight week period in a double blind, between-subjects design.

Results: The complete results of the trial will be presented at this conference. As this trial is yet to be accepted for publication, we do not report results within this abstract. We will discuss results, moderating factors, and limitations of the current study at the time of presentation.

Conclusions: The results provide data on 50 patients with autism recruited into an oxytocin nasal spray treatment trial. This trial demonstrates whether oxytocin nasal spray improves social cognition and behavior in autism. It provides valuable data on the potential of a new treatment for autism spectrum disorders.

162.102 102 Intranasal Oxytocin for the Treatment of Core Symptom Domains in Children and Adolescents ASD: A Maximum Tolerated Dose Study. E. Anagnostou*¹, S. Jacob² and J. A.

Brian³, (1)*Bloorview Research Institute*, (2)*University of Illinois at Chicago*, (3)*Holland Bloorview/ Sick Kids*

Background: There is considerable evidence of the involvement of oxytocin in modulation of social cognition/ perception systems as well as social reward. Early human data suggests that manipulation of the oxytocin system impact social cognition/ perception and may have therapeutic potential in ASD. Little is known about the maximum tolerated dose in children with ASD and the sensitivity of existing measures to capture change.

Objectives: We conducted a Maximum Tolerated Dose (MTD) pilot study of intranasal oxytocin in children and adolescents 10-18 years of age and explored effects on safety, social perception cognition and function and anxiety.

Methods: 25 children and youth with ASD, with diagnosis confirmed by expert clinician using ADOS, ADI-R and clinical information were enrolled into the study. They were exposed to active medication for 12 weeks and followed for 24 weeks. MTD design involved assignment in the following dose range: 0.2, 0.26, 0.33, 0.4 IU/kg/dose, in 3 patient increments. Safety was measured using the SMURF, vital signs, safety bloodwork and EKG. Potential efficacy was measured by exploring effects on social cognition / perception (LETS FACE IT, Irony and Empathy), the social responsiveness scale, and anxiety (CASI).

Results: Statistically significant improvements were noted within group in aspects of social cognition / perception [face recognition ($p = 0.002$) as measured by the LFI, and theory of mind ($p = 0.06$) as measured by the Irony and Empathy task]. Improvements were noted in overall symptoms as measured by the SRS ($p = 0.003$), and anxiety as measured by the CASI ($p = 0.006$). Effects were maintained after 3 months of oxytocin discontinuation. Side effects were mild. No serious adverse events were reported at any of the dose categories.

Conclusions: Preliminary data supports that manipulation of oxytocin system over a 12 week period is safe, and may produce therapeutic effects in terms of social perception / cognition and also leads to anxiolytic effects. Larger

studies are required to further examine such effects

162.103 103 Association of Serum Cytokine Levels, Treatment Response, and Weight Gain in Children with Autism Spectrum Disorders Following 8 Weeks Treatment of Risperidone. J. E. Choi^{*1}, P. Ashwood², F. Widjaja¹, M. Careaga² and R. Hendren¹, (1)*University of California, San Francisco*, (2)*The M.I.N.D. Institute, University of California, Davis*

Background: Children with Autism Spectrum Disorders (ASD) frequently exhibit irritability. Atypical antipsychotics are shown to decrease behavioral disturbances in this population. Recent studies sought to identify predictors of clinical improvement and side effects in children with ASD following treatment with risperidone. In this exploratory analysis, our aim is to determine predictors of response to treatment and of weight gain by comparing baseline and changes in cytokine levels in an 8 week risperidone study.

Objectives: Determine if response to treatment and weight gain following 8 weeks of risperidone treatment is associated with baseline serum levels and changes in cytokine levels.

Methods: We used data of the plasma levels of 27 different cytokines from 41 children who had an initial Aberrant Behavior Checklist Irritability (ABC-I) subscale rating of ≥ 18 . Subjects were uptitrated to a daily total of 1.5 mg of risperidone over 8 weeks. Outcome measures were % decrease in ABC-I (%ABC-I) scores and Clinical Global Impression-Improvement (CGI-I) score. Subjects were overall responders to treatment if they had a decrease in %ABC-I $> .25$ and a CGI-I of "very much improved" or "much improved". Cytokine analysis was performed using multiplex assays (Millipore) according to manufacturer's recommendation and read on Luminex 100™ platform. Weight gain was represented through change in z-scores of anthropomorphically-adjusted BMI distributions. We assessed normality of the data and identified outliers and did not adjust p-values for multiple testing for this exploratory analysis. Correlations were determined using Spearman's rank correlation coefficient, differences between baseline and post-treatment values were determined using Wilcoxin sign rank tests and changes between responder and nonresponder

groups were determined using Mann-Whitney tests.

Results: D %ABC-I ($p < .00001$) was significantly decreased following 8 weeks of treatment. Plasma levels of Eotaxin ($p = .0005$) and MCP1 ($p = .02$) was significantly decreased. There are no significant correlations between D%ABC-I and change in cytokines levels. Baseline IL-15 is a significant predictor of ABC-I response only ($p = .04$) with an adjusted (sex, age) odds ratio of 3.5. The median values of DIL-5 ($p = .006$) are significantly higher in the overall responder group compared to nonresponders and DIL-15 ($p = .07$) is marginally higher. In comparing the highest responders (decrease %ABC-I $> .60$) to nonresponders, median values of DIL-15 ($p = .04$) are significantly higher and DIL-5 ($p = .07$) is marginally higher. There are no differences in baseline measure. There is no association between weight gain and response. Weight gain is negatively correlated with DIL-5 ($p = .02$) and DINFa2 ($p = .01$). We found no baseline predictors of weight gain.

Conclusions: Responders had a greater increase in IL-5 compared to nonresponders. Greater overall improvement is associated with significant increases in IL-5 and IL-15. Those with higher levels of baseline IL-15 are more likely to have a reduction in irritability symptoms alone. There is a significant decrease in Eotaxin and MCP1 levels following 8 weeks of risperidone treatment. Previous studies report increased MCP-1 and Eotaxin levels in children with autism when compared to controls and are associated with higher ABC-I scores. The effects on cytokines due to weight gain and baseline cytokine levels are not predictive biomarkers of weight gain.

162.104 104 Pharmacotherapy in Autism: A Prospective One-Year Study with Risperidone. J. Almeida^{*1}, S. Mouga², C. Marques¹, F. Caramelo³, J. M. Pereira³, A. M. Vicente⁴, F. Duque¹ and G. Oliveira¹, (1)*Hospital Pediátrico Carmona da Mota (HP) – Centro Hospitalar e Universitário de Coimbra (CHUC)*, (2)*Faculdade de Medicina – Universidade de Coimbra*, (3)*University of Coimbra*, (4)*Instituto Nacional de Saúde Doutor Ricardo Jorge*

Background: Autism is described by impairments in social interaction, communication and stereotyped/repetitive behaviours. Besides these core features, are frequently associated symptoms of anxiety, agitation, aggression,

inattention, hyperactivity, self-injury and sleep problems. When non-medication therapies are not enough to control disruptive behaviours (DB), pharmacotherapy is often required. Risperidone is the most studied new generation neuroleptic in autism. There are several short-term trials and one long-term follow-up study (six months) that demonstrated the effectiveness in the management of behaviour dysregulation in autism.

Objectives: The objective of this research was to explore the effects of risperidone on DB in subjects with autism for period of time of one year.

Methods: 47 subjects with autism were included, medicated with risperidone for one year. Drug effectiveness in DB was evaluated using Autism Treatment Evaluation Checklist (ATEC) at baseline and at defined times (T) after start of risperidone therapy (1, 3, 6 and 12 months). The reduction in average scores indicates significant clinical improvement. Inclusion criteria were: diagnosis of autism (ADI-R/ADOS positive results); no profound intellectual disability (Global Intellectual/Developmental Quotient > 35 or mental age > 18 months); severe DB with no response to non-medication treatments (presence of two or more DB with Moderate Problem or Serious Problem classification at ATEC: sleep problems; hyperactive; hits or injures self; hits or injures others; destructive; anxious/fearful; shouts or screams; often agitated); without any psychotropic medications for at least 3 months. Statistic analysis (SPSS17) was performed comparing the variation of scores in each assessment times with ANOVA or Friedman repeated measures tests. Significance level (σ) = 0.05.

Results: 39 of 47 (83%) subjects completed one year of medication with risperidone (30M/9F:3.3/1). Although the mean risperidone dose was increased progressively throughout the year, the largest increase was found from the 3rd (1,29 \pm 0,71mg/day) to the 6th month (1,36 \pm 0,66mg/day). There was a significant progressive reduction in the global average score of ATEC in T1,T3,T6,T12 after baseline (T0), beginning with a score = 68.87 (T0) to a minimum = 33.87 (T12). This improvement score was 51% and showed statistical significance

($p < 0.0001$). The average scores in subscales of ATEC (I-Speech; II-Sociability; III-Sensory/Cognitive Awareness; IV-Health/Physical/Behaviour) have revealed significant changes over the year of treatment (T0-T12: $p < 0.0001$), this improvement was more evident in subscale-IV. The reduction in the average score of disruptive behaviour during the T0-T1 of medication (T0=23.44 to T1=12.1) was 48%. The decrease in DB continued to register until T12, showing an improvement of 73%. In the Subscales I, II and III improvement between T0-T12 was 34%, 49% and 31%, respectively. In any of the cases excessive sedation or extrapyramidal side-effects were verified.

Conclusions: These findings demonstrate that risperidone, in low doses and with minor adjustments, can rapidly improve some symptoms often associated with autism, particularly in the DB. This benefit, which occurred as early as T0-T1 of treatment, was increased over a year. There was also a significant improvement in the other subscales, but on a lower degree. As in other previous studies, the results obtained confirm the rapid efficacy of risperidone in the treatment of DB in autism, maintaining a positive response in the long term which discourages its suspension.

162.106 106 Efficacy and Safety of Lisdexamfetamine Dimesylate in Adolescents with Attention-Deficit/Hyperactivity Disorder. T. Banaschewski¹, M. Gasiot², L. Squires², R. Bloomfield³ and D. Coghill⁴, (1)Central Institute of Mental Health, Medical Faculty, Mannheim, University of Heidelberg, (2)Shire Development LLC, (3)Shire Pharmaceutical Development Ltd, (4)University of Dundee

Background:

The prodrug stimulant lisdexamfetamine dimesylate (LDX) is an effective, once-daily treatment for patients with attention-deficit/hyperactivity disorder (ADHD).

Objectives:

To evaluate the efficacy and safety of LDX in adolescent patients with ADHD in a European, randomized, double-blind, phase 3 trial. Results are compared with those of an earlier US-based study of LDX in adolescent patients with ADHD.

Methods:

SPD489-325 was a European, 7-week, randomized, placebo-controlled trial of an optimized daily dose of LDX (30mg, 50mg or 70mg) in children (aged 6–12 years) and adolescents (aged 13–17 years) with ADHD; osmotic-release oral system methylphenidate (OROS-MPH, 18mg, 36mg or 54mg) was included as a reference arm. SPD489-305 was a US-based, 4-week, forced-dose titration, double-blind study, in which adolescents (aged 13–17 years) with ADHD were randomized equally to once-daily LDX 30mg, 50mg or 70 mg or placebo. For both studies, the primary efficacy measure was the change from baseline in ADHD Rating Scale version IV (ADHD-RS-IV) total score at endpoint (last on-therapy, post-randomization visit). Safety assessments included, but were not limited to, treatment-emergent adverse events (TEAEs) and vital signs.

Results:

In study SPD489-325, a total of 336 patients were randomized and 88 adolescents (aged 13–17 years) were included in the full analysis set (FAS). At endpoint, placebo-adjusted least-squares (LS) mean changes from baseline (95% confidence interval [CI]) in ADHD-RS-IV total scores in adolescents were: LDX, -20.8 (-25.7, -16.0); OROS-MPH, -8.1 (-13.0, -3.3) ($p < 0.001$ for both comparisons versus placebo). Consistent with the known effects of stimulant treatment, TEAEs reported by $\geq 10\%$ of adolescents receiving LDX included decreased appetite, headache, decreased weight and insomnia. In SPD489-305, 314 adolescents were randomized and 309 were included in the FAS. At endpoint, the differences (LDX - placebo) in LS mean changes from baseline (95% CI) in ADHD-RS-IV total scores for LDX were: 30mg, -5.5 (-9.7, -1.3); 50mg, -8.3 (-12.5, -4.1); 70mg, -7.9 (-12.1, -3.8) ($p < 0.01$ for each comparison versus placebo). TEAEs reported by $\geq 10\%$ of adolescents receiving LDX were decreased appetite, headache and insomnia.

Conclusions:

LDX was effective and generally well tolerated in a subgroup of patients aged 13–17 years with ADHD in this European phase 3 trial. Results were generally consistent with those of an earlier, US-

based clinical trial of LDX in adolescents with ADHD.

162.107 107 Medication Use in Adolescents and Adults with ASD: The Role of Clinical, Parent, and Service Need Factors. J. K. Lake*¹, Y. Lunskey² and J. A. Weiss³, (1)*University of Toronto*, (2)*Centre for Addiction and Mental Health*, (3)*York University*

Background: Mental health and behavioural issues are common in individuals with autism spectrum disorders (ASD), and primarily treated through pharmacology. Recent studies estimate that over one half of adults with ASD are prescribed psychotropic medications, with over one quarter taking three or more (Aman, et al., 2003; Lake et al., 2012; Langworthy-Lam, et al., 2002). Psychiatric support, greater age, group home residence, and more severe symptoms of autism are all associated with increased medication use (Aman, et al., 2003; 2005; Lake et al., 2012). Despite this, few studies have examined what predicts medication use in adolescents and adults with ASD, particularly from a service utilization, clinical need, and parent need perspective.

Objectives: To identify profiles and predictors of medication use in terms of clinical need, parent need, and service utilization factors.

Methods: As part of an online survey examining health service utilization patterns among individuals with ASD, 463 parents completed demographic and clinical measures related to their child's service use, comorbid medical and psychiatric conditions, medication use, risk behaviours, severity of ASD, history of previous hospitalizations, and parental wellbeing (e.g., burden, worry, knowledge).

Results: Preliminary analyses revealed that 53% of adolescents and adults with ASD were taking at least one psychotropic medication, with over one half of this group prescribed antipsychotics. Approximately 50% of those taking psychotropic medications were taking antidepressants, 33% stimulants, and 19% anxiolytics. Over one half of adolescents and adults prescribed psychotropic medications were taking 2 or more of these drugs (polypharmacy), and 36% of these individuals had no other diagnosis in addition to ASD. At the bivariate level, both clinical need (psychiatric comorbidity, aggression, and self-injury) and

service utilization (forensic involvement, having a family physician, and past emergency department visitation) were associated with polypharmacy. Parent variables associated with polypharmacy included receiving family therapy/counseling support. Findings related to other parent variables (e.g., burden, worry, knowledge) will be explored.

Conclusions: Over one quarter of the current sample was prescribed 2 or more psychotropic medications, with antipsychotics prescribed most often. A number of clinical, parent, and service utilization variables were associated with psychotropic medication use and polypharmacy. Findings from this study are relevant to improving the mental health care of adolescents and adults with ASD by providing clinicians, individuals with ASD, and caregivers of individuals with ASD, with current, evidence-based information on medication use in this population. Knowledge may also help families, clinicians and individuals with ASD anticipate the use of medication, explore strategies to best monitor medication use, and consider alternative or adjunctive treatments.

162.108 108 Clinical and Laboratory Results From Randomized Controlled Trial of Methylcobalamin Injections for Children with Autism. F. Widjaja*¹, J. E. Choi¹, S. Bent¹, S. J. James² and R. L. Hendren¹, (1)*University of California, San Francisco*, (2)*University of Arkansas for Medical Sciences*

Background:

Methylcobalamin (MB12) injection may act as a superoxide free radical scavenger (antioxidant) to decrease homocysteine levels and chronic oxidative stress in children with autism.

Objectives:

To determine if methylcobalamin supplementation can improve behavioral measures in children with autism; if improvement is associated with biomarkers in methylation pathway; and if a predictor of positive behavioral response can be found in this pathway.

Methods:

This is an 8-week, double-blind, randomized, placebo-controlled study of injectible methyl B12 in 50 children with autism, followed by an optional open-label extension study lasting eight to 16 weeks. Behavioral assessments and blood samples are obtained at baseline, weeks 8 and 16.

75 mcg/kg methylcobalamin or placebo subQ were administered by parents once every 3 days for 8 weeks. The primary outcome measure was the CGI-I (Clinical Global Impression-Improvement).

Secondary measures included the ABC (Aberrant Behavior Checklist), BASC (Behavior Assessment System for Children), CCC (Children's Communication Checklist), SRS (Social Responsiveness Scale) and PDDBI (Pervasive Development Disorder Behavior Inventory).

Results:

Fifty subjects (40 males, 10 females; aged 2 year 11 months to 7 year 9 months) were randomized in the study. Forty four subjects have completed the study and six are currently ongoing. Plasma B12 levels were not deficient at baseline but were in high normal range (~900 pg/ml). Methyl B12 injections were well tolerated. 19 responders (43%) were identified out of the 44 subject who completed the study. 13 of them were on active B12 and 6 were on placebo. Chi-square analysis of CGI-I responder status compared to baseline was marginally significant ($p=.06$). Responders were defined as having CGI Improvement as very much improved (1) or much improved (2). Mean values of the CGI-I are significantly lower in active B12 group compared to the placebo group (t-test, $p=.01$).

Compared to the placebo group, the MB12 group demonstrated significant improvement after 8 weeks on the ABC irritability subscale ($p=.01$), the ABC hyperactivity subscale ($p=.02$), the BASC Externalizing subscale ($p=.05$), the BASC Behavioral Symptoms Index ($p=.08$), the CCC Syntax ($p=.02$) and the CCC Initiation subscale ($p=.05$). Higher homocysteine & SAH predicts positive behavior response ($p=.02$). Lower SAM/SAH predicts positive behavior response ($p=.03$). Within the methylcobalamin group, homocysteine and SAH levels were significantly reduced from baseline after treatment. Homocysteine levels were positively correlated with SAH only at levels $\geq 9 \mu\text{mol/L}$ in the methylcobalamin treated group.

Conclusions:

Methylcobalamin injections (75 $\mu\text{g/Kg}$) three times weekly significantly lowered the mean CGI-I

score, the ABC irritability and hyperactivity subscales and significantly reduced plasma homocysteine levels compared to placebo in children with autism. Data from this study support the potential usefulness of methyl B12 for treating irritability in children with autism. Predictors of positive behavioral response included Homocysteine, SAH and SAM/SAH ratio. Methylcobalamin may be acting as a free radical scavenger.

162.109 109 Biomarkers of Change in Social Impairment and Aberrant Behaviors Among Children with Autism. S. L. Logan*, L. A. Carpenter, L. B. King, C. A. Cheely, J. Charles, W. Jenner, I. Singh and J. S. Nicholas, *Medical University of South Carolina*

Background: Inflammation, as evidenced by abnormal cytokine levels, may interfere with neuronal development and activity resulting in social and behavioral impairments. Studies show that both the core deficits and associated aberrant behaviors in autism may be associated with altered cytokine levels, and fatty acid supplementation may alter cytokine production and release. The extent to which changes in cytokine levels are associated with changes in core symptoms and behaviors of autism is not known.

Objectives: To examine associations between fatty acid supplementation, cytokine level changes, and changes in behavior among children aged 5 to 12 years with ADOS-confirmed autism.

Methods: Plasma fatty acid and cytokine measures (TNF alpha, IL-1 beta, IFN gamma, IL-10) were analyzed pre- and post-intervention of 12 weeks of unsaturated fatty acid supplementation ($n=58$). These measures were correlated with changes on several behavioral scales: the Aberrant Behavior Checklist (ABC) for parents, the Pervasive Developmental Disorder Behavior Inventory (PDD-BI), and the Clinical Global Impressions (CGI) Scale. Pearson's correlation coefficients were calculated for changes in fatty acid and cytokine levels, and changes in behaviors based on the ABC, PDD-BI, and CGI scores.

Results: Significant correlations between behavior change scores and cytokine change scores were found. Changes in IFN Gamma levels were associated with a broad range of changes in

scores on both the PDD-BI and ABC, including changes in aggressiveness, arousal regulation problems, approach/withdrawal problems, expressive language, expressive social communications abilities, specific fears, learning, memory, and receptive language, receptive/expressive social communications abilities, ritualisms/resistance to change, semantic pragmatic, social approach behaviors problems, social pragmatic problems, hyperactivity/noncompliance, stereotypic behavior, and inappropriate speech. Changes in sensory/perceptual approach scores were also associated with changes in IL-1 beta levels. TNF alpha and IL-10 changes were not correlated with behavioral changes in any domain. Changes in EPA levels also significantly correlated with changes in autism composite scores.

Conclusions: The correlated changes in cytokine levels as biomarkers of inflammation with changes in behavioral scores extends previous findings that autism is associated with various immune system abnormalities. Results may provide a clue as to the mechanism of how these behavioral changes occur, and suggest that more direct methods of reducing inflammation in autism may be appropriate for further study.

162.110 110 Dietary Patterns Among Children with Autism in Oman:

A Study Protocol. N. M. Al-Kindi*, M. Al-Shafae, M. I. Waly, M. Al-Sharbat, A. Ouhtit, M. M. Al-Khaduri, S. al-Adwai and Y. M. Al-Farsi, *Sultan Qaboos University*

Background:

Prior studies conducted in Oman indicated relatively high prevalence of malnutrition and micronutrient deficiencies among children with ASD compared to non-ASD children. Nonetheless, little information is available regarding the food items being accepted by these children or the possible factors contributing to their feeding problems.

Objectives:

The overall aim is to carry out a comprehensive assessment of nutritional wellbeing of children with ASD in Oman. Specific objectives include: 1) Evaluation of dietary adequacy; 2) Investigation of nutritional risk factors such as food selection,

feeding problems, low physical activity, and medication/food supplement.

Methods: < style="text-align: left;">Participants will be caregivers of 150 Omani children with ASD aged 3-14 years, and caregivers of 150 non-ASD controls. Cases and controls will be matched according to age, gender, and ethnicity of children. Data of interest include demographic information, anthropometric measurements, and dietary and nutritional information. Dietary assessment will be done using the following tools: 1) Gilliam Autism Rating Scale (GARS); 2) Children's Eating Behavior Inventory (CEBI); 3) Food Preference Inventory (FPI); and 4) The 3-day food record.

Results:

A pilot study has been completed based on 20 cases and 20 controls. The preliminary results indicated high response and cooperation rates among participants. The data collection tools have been standardized to the local set up. Piloting assessment indicated high reliability; and high validity parameters (content, construct, and criterion).

Conclusions:

Study protocol for a comprehensive nutritional assessment of children with ASD in Oman has been designed. Initial piloting indicated high applicability of study tools to local context.

162.111 111 The Therapeutic Breakfast As a Tool for Improving Eating Behaviors and Communication Skills in Children with ASD. Y. Evron*¹, A. Jokel², Y. Shmaya³, O. Leon³, S. Shefer⁴ and L. V. Gabis⁵, (1)*Tel Hashomer, Safra Children's hospital*, (2)*Tel-Hashomer, Safra Children's Hospital*, (3)*Tel Hashomer, Safra Children's Hospital*, (4)*The sheba medical center The Weinberg child development center*, (5)*Weinberg Child Development Center*

Background: Children with Autism Spectrum Disorders (ASD), may exhibit, in addition to communication difficulties, behaviors such as insistence on sameness, inflexible tendencies and a need for a strict routine (Myers & Johnson, 2007). Though feeding disorders are not among the diagnostic criteria for autism listed in the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR), many of these individuals

exhibit different eating habits including sensory based issues (sensitivity to smell, taste, texture etc.) and/or the need for a constant routine (eating only at fixed times or fixed foods). In many cases, in order to avoid struggles with their child during meals, parents of children with autism tend to offer their child a fixed menu, thus maintaining food selectivity and a limited diet.

Objectives: The purpose of the "Therapeutic Breakfast" is to encourage improvement in eating behaviors and communication skills among children with autism.

Methods: This study included 13 children, ages 4-6, diagnosed with PDD-NOS or Autism who participated in a therapeutic breakfast program on a weekly basis for 20 weeks. The "Therapeutic Breakfast", carried out in groups of up to 8 children, includes a multidisciplinary team (Dietician, OT, SLP, Psychologist and Developmental Pediatrician) providing individual intervention for each child. Parent involvement is an integral part of the program to ensure carryover at the home. Participants are gradually exposed to a variety of foods throughout the program in order to encourage healthy eating habits. In addition to the eating experience, the group provides an opportunity for communication around the table. Fifteen observations on each child were collected and consisted of the following variables: independent eating, use of utensils, variability of food intake, initiation of communication, adaptive response to others, sitting near the table and body posture while sitting. A five-level Likert scale was used for rating where the highest performance was scored as 5 and the lowest performance was scored as 1. The first and last observations for each variable were compared using a t-test.

Results: Results suggest that initiation of communication and body posture while sitting were found to have improved significantly following our intervention. For the other 5 variables there was a trend for improvement, although not statistically significant.

Conclusions: The Therapeutic Breakfast improves eating behaviors and communication skills in children with ASD. It is necessary to evaluate and address the eating behaviors of these children as part of their care. A larger randomized controlled

study is needed in order to establish the efficacy of the "Therapeutic Breakfast" as a therapeutic tool for children with ASD. The "Therapeutic Breakfast" model will be presented as well as ideas for food exposure used by the professional team.

162.112 112 Attention Preference of Animals in Children with Autism Spectrum Disorders --- an Eye-Tracking Study. C. Wang*¹, Y. Yu², X. Zhou² and M. M. Hussey³, (1)*Nankai University*, (2)*Nankai University*, (3)*Beijing Normal University*

Background:

Animal-assisted therapy (AAT) began to be used for treatment of individuals with autism spectrum disorders (ASD) in the 1990s. Clinical reports have suggested that this therapy is indeed effective for patients with ASD. However, in general, much of the information available about AAT is qualitative or anecdotal, and studies evaluating the effectiveness of AAT lack of scientific control and rigor. As a result, AAT has not yet had the scientific evidence base to make it a widely used in the treatment for ASD.

Objectives:

The objective of the study is to determine if AAT can find its cognitional support in the treatment for ASD by assessing the differences in attention features between typically developing (TD) children and children with ASD when they are looking at the social interaction scenes which contain both a human and an animal.

Methods:

Children aged 5 to 10 years (14 with an ASD and 20 TD children) were presented with 24 natural social interaction videos, which are chosen from TV dramas or documentary films as well as made by ourselves. These videos are divided into three types: a human interacting with a human (2 videos), an animal interacting with an animal (12 videos), and a human interacting with an animal (10 videos). Using the preferential looking paradigm, total fixation duration, and the number of saccades within each movie type were examined using eye tracking technology. The percentage of visual fixation time to 3 regions of interest were compared between ASD and TD

groups: interaction, no interaction area of human or animal, and background (the area not containing human or animal).

Results:

The results showed that: a) compared with TD children, children with ASD have significantly longer fixation on animals; b) when looking at animals, children with ASD spent more time fixating on the heads of animals instead of bodies compared with TD; c) children with ASD spent more time looking at the dog and dolphin than other kind of animals though we do not know why.

Conclusions:

By demonstrating eye-tracking behaviors in the context of human-animal social interaction, our study can give cognitive support for the use of AAT in treatment for some individuals with ASD.

162.113 113 Sensory Integration - A Randomized Trial for Children with Autism. R. Schaaf* and T. Benevides, *Thomas Jefferson University*

Background: Sensory hypo and hyper-responsivity have been described in the autism literature since the disorder was first identified. Current estimates show that between 70-96% of children with Autism Spectrum Disorders (ASD) demonstrate these sensory features (Ben-Sasson, et al 2009), and they are now proposed to be included as a core feature for diagnosis of Autism Spectrum Disorders (ASD) under the Restricted and Stereotypic Behavior criteria in the DSM 5 (APA, 2012). As such, objective markers of these features have new and important relevance for diagnosis and treatment of ASD. Our work, to date, shows these sensory differences create social isolation for families and their children, significantly restricting full participation in daily activities. Consequently, interventions to address sensory differences are among the most often requested services, and, although data on their effectiveness is promising, more rigorous trials are needed.

Objectives: To determine if occupational therapy using sensory integration (OT/SI) improves adaptive behavior (as measured by individualized goals and standardized assessments) and

decreases sensory features. We previously completed a feasibility study showing that the intervention is safe, feasible to deliver, acceptable to families and that interventionists were able to obtain adequate fidelity (Schaaf, Benevides, Kelly & Mailloux, 2012). All subjects were well characterized using the ADOS and ADI-R.

Methods: Thirty-two children diagnosed with autism spectrum disorders, between the ages of 4-8 years were enrolled in the study. Following phenotypic characterization (diagnosis of autism using ADOS-G, ADI-R and a cognitive assessment), subjects were assessed to identify their sensory dysfunction, and if eligible, were enrolled into the study. Following pre-test assessment, individualized goals were developed using assessment findings and parent-identified goals using Goal Attainment Scaling methodology. Randomization to either OT/SI or Usual Care (UC) occurred using stratified blocks based on ASD severity and cognition. Children assigned to OT/SI received 30 treatments over a 10 week period. Intervention followed a manualized protocol that operationalized the principles of sensory integration. Primary and secondary outcomes were Goal Attainment Scale rating, Pervasive Developmental Disorder Behavioral Inventory (PDDBI) scores, Pediatric Evaluation of Disability Inventory (PEDI), and the Sensory Integration and Praxis Tests obtained at pre and post intervention by independent, blind evaluators.

Results: Parents of children in the treatment group reported significantly higher goal attainment ($p = .003$) and on the PEDI, children were reported to have significantly greater independence in their self-care ($p = .039$) and social functions ($p = .008$). In addition, sensory behaviors measured by the PDDBI decreased more in the treatment group in comparison to the controls and approached significance ($p = .064$).

Conclusions: The findings from this trial show that occupational therapy using sensory integration principles significantly improves attainment of individually identified functional goals, and has an impact on independence in self-care and socialization. In addition, this intervention shows a tendency to decrease parent-reported sensory behaviors.

162.114 114 Pressure Garments as a Regulator of Behavior of Children and Adolescents in Autism Spectrum Disorders (ASD). A. Lehto*¹, T. Ukura², I. K. Moilanen³ and H. Ebeling⁴, (1)*Institute of Clinical Medicine, University of Oulu*, (2)*Institute of Clinical Medicine, University of Oulu*, (3)*University of Oulu*, (4)*University and University Hospital of Oulu*

Background:

Weighted blankets and vests are commonly used as a treatment for autism, and this method has been found to work well. They have also been helpful in calming children with motoric restlessness and for improving body awareness.

Pressure garments are a convenient way to generate a feeling of pressure. They are snugly fitting clothes, which apply adjustable pressure on different areas of the body. Each garment is tailor-made for each individual, and considerable planning goes into the design and selection of materials. The focus is on comfort, but also on the external product design. In this study, pressure garments with long pants and sleeves were used as intervention.

Objectives:

This study investigated whether pressure garments could benefit children with ASD behavior.

Methods:

The study had 32 participants with ASD behavior aged 9 to 23 years. Each individual exhibited challenging and/or aggressive behavior. Only six of participants were without a comorbid learning disability diagnosis. 87.5% of participants were attending primary education (n=28).

The study design was carried out as follows in late 2008: Initially, respondents (parents, teachers, nurses) observed participants for a period of one month after which they completed questionnaires (survey 1). Participants began to use their custom-made pressure garments as they became available. The first participants received their garments at the end of January and the last ones in early February. Participants were given the following instructions: In the morning, the

pressure garments are dressed over underwear, and under regular clothes. The garments are used continuously for 7 hours daily, and then removed. Participants used the garments until the end of May 2009. Subsequently, we assessed participants with the same questionnaire packet that was employed at the beginning of the study (survey 2), including the PSYTO-AU-questionnaire, a modified version of the psychosocial functioning scale (PS-TKA) for mentally disabled persons with autism.

Results:

Despite noticeable between-subject variation, evidence suggests that the pressure garments significantly modulated ASD behaviors in some individuals according to PSYTO-AU-questionnaire, and in general, a trend for the overall efficacy of these garments is observable. The simple linear regression model demonstrate that the effect of using pressure garments were most apparent in social skills ($R^2=23\%$) $p < 0.001$, social relationships ($R^2=24\%$) $p < 0.001$ and processing sensory information ($R^2=30\%$) $p < 0.001$. The regression model gives the best explanation of these rates which are statistically significant.

Conclusions:

Pressure garments may be beneficial when individuals with autism integrate into society and thereby avoid social exclusion. Pressure garments may have a possible role in the multimodal treatment of ASD.

162.115 115 Impact of Dog Assisted Therapy On Children with Autism Spectrum Disorders. R. Maxim*¹, M. W. Baig², D. Zand³, A. C. Vercellone³, R. Grimmer², M. Bultas⁴ and H. Matsuo³, (1)*Saint Louis University School of Medicine*, (2)*SSM Cardinal Glennon Children's Medical Center*, (3)*Saint Louis University*, (4)*Saint Louis University School of Nursing*

Background: Given core deficits in language, social interaction and play, children with Autism Spectrum Disorder (ASD) may benefit across multiple contexts from incorporating trained dog interactions into their regular therapy routines. There are very few small studies showing that the presence of a therapy dog can facilitate verbal and nonverbal communication as well as decrease

anxiety, particularly in children with autism spectrum disorders.

Objectives: To assess the impact of a therapy dog on anxiety, communication, shared enjoyment, compliance and attention in children with ASD.

Methods: In this retrospective study we reviewed the videotaped clinical session and medical records of 22 patients enrolled in the dog therapy clinic at a large Midwestern city children's hospital. The visit consisted of the child's participation in a Physical Examination task, Blood Test task, Make a Basket task and several pretend play tasks. The tasks were completed with and without the therapy dog. Each task incorporated the use of the therapy dog in facilitating reenactment of the targeted routines. Aberrant Behavior Checklist (ABC), the Dog Therapy Questionnaire, and the Preferred Activities Questionnaire were completed by parents before the session. We assessed the parental expectations as well as the perceived benefits of incorporating dog interactions into their child's therapy session through the Feedback Questionnaire which was completed by the parent at the end of the observed sessions.

Results: After excluding the subjects from whom we were unable to obtain parental consent, the final sample consisted of 22 children with an age range of 2-14 years, mean age 5.73 years, 1 SD=3.298. There were 72.7% males, and 63.6% Caucasians, 13.6% African Americans, and 22.7% children with other racial backgrounds. Most common behavior problems reported by parents were temper outbursts, abnormal and repetitive movements, disobedience, and short attention span. Behavior problems reported by ten or more parents were defined as common problems. The effect of dog therapy on child's behavior as reported by parents was classified into three groups: improvement (in 63% of the children), no change (in 27% of the children) and partial improvement (in 9.1% of the children). Although Kruskal-Wallis test of comparison of age difference among three groups was not significant, older children tended to show more improvement than younger children. Parents who reported improvement in their children's behavior mentioned "their child had improved attention,

"looked happier," and "more emotionally connected to people".

Videotape analysis of child behavior with and without the dog will be available for the final presentation.

Conclusions: Utilizing a dog in the treatment process may help children diagnosed with ASD to become more compliant, attentive, social, and adapted to their environment.

162.116 116 Behavioral and Physiological Changes Due to the Effects of Ambient Prism Lenses and Visuo-Motor Exercises in Autism. B. A. Dombroski^{*1}, M. Kaplan², B. Kotsamanidis², S. M. Edelson³, G. Sokhadze¹, E. M. Sokhadze¹ and M. F. Casanova¹, (1)University of Louisville, (2)Center for Visual Management, (3)Autism Research Institute

Background: A common comorbidity of autism includes a dysfunction within the ambient visual system that negatively affects peripheral vision and causes deficits in attention, hand-eye coordination, balance, and gross motor movement. Ambient vision is necessary for control of anatomical movement involved in spatial orientation and proprioception. Dysfunction of this system impairs the ability to process environmental cues used to control gait, posture, movement, and speech. Loss of spatial orientation negatively affects the vestibular system, which leads to the development of adaptive responses that are consistent with the behavioral symptoms observed in autism.

Objectives: This study uses physiological recordings and clinical surveys to evaluate the effects of corrective ambient prism lenses and daily visuo-motor therapy on aberrant and repetitive behaviors and body coordination.

Methods: In this study, twenty autistic individuals (mean age 12.5) were recruited, evaluated, and individually prescribed corrective ambient prism lenses. Next, a six-month daily vision therapy protocol was implemented. Patients were instructed to wear the corrective ambient prescription lenses all day, except when vision therapy procedures instructed the patients otherwise. Daily vision therapy procedures included exercises that required the patients to wear disruptive prism lenses and occasionally

red/green lenses. The combination of the lenses and tasks were used to address problems involved in balance, visual organization, and depth perception. Empirical behavioral data was reported using the Autism Behavior Checklist (ABC) and Repetitive Behavior Scale (RBS). Physiological variables of autonomic reactivity recordings included measurements of Heart Rate (HR), Heart Rate Variability (HRV), Skin Conductance Level (SCL), and Skin Temperature (ST), which were taken while the subject was watching scenes from the classic Disney film, "The Lion King," to evoke emotional responses.

Results: Autonomic reactivity recordings for Heart Rate Variability (HRV) and Skin Conductance Level (SCL) had significantly decreased after four months of wearing corrective prescription ambient prism lenses compared with baseline recordings showing that sympathetic arousal went down in these individuals. Empirical behavioral data was reported using the Autism Behavior Checklist (ABC) and Repetitive Behavior Scale (RBS). After four months, two out of five scaled scores were significantly reduced according to the ABC. In particular, scores decreased in Irritability ($t = 2.97$; $p = 0.014$) and Hyperactivity ($t = 3.396$; $p = 0.007$) compared to baseline scores. According to the Repetitive Behavior Scale (RBS), three out of six subscale scores were significantly different. These subscale scores included: Stereotypic Behavior ($t = 3.47$; $p = 0.010$), Compulsive Behavior ($t = 3.49$; $p = 0.010$) and overall Total Score ($t = 2.70$; $p = 0.031$) compared to baseline scores.

Conclusions: Results of this study showed that corrective ambient prism lenses combined with daily visuo-motor therapy reduced autistic behaviors (according to ABC and RBS rating scores) and enhanced autonomic reactivity to emotional stimuli in ASD individuals.

162.117 117 Vision Testing of Children and Adolescents with ASD: What Are We Missing?. R. A. Coulter^{*1}, Y. Tea¹, A. Bade¹, G. Fecho¹, D. Amster¹, E. Jenewein¹, J. Rodena¹, K. K. Lyons², G. L. Mitchell³, N. Quint¹, S. Dunbar¹, M. Ricamato², J. Trocchio⁴, B. H. Kabat³, C. Garcia¹ and I. Radik¹, (1)*Nova Southeastern University*, (2)*Private practice*, (3)*Private consulting practice*, (4)*CasaBlanca Academy*

Background:

Many studies have reported on visual function in individuals with autism spectrum disorder (ASD) (Simmons, et al., 2009). Vision screening has been compared in ASD and typically developing (TD) peers (Milne, et al., 2009). To date, no study has reported results of vision testing within a comprehensive eye examination protocol in the ASD population nor compared that to a sample of TD peers. This information is needed to diagnose and manage vision problems and to establish a standard of care for ASD patients.

Objectives:

An eye examination protocol was designed to accommodate the communication and sensory challenges associated with ASD. This study compared vision testing in this protocol for ASD patients to that of TD peers.

Methods:

61 children and adolescents ages 9 to 17 years and who were TD ($n=27$) or had ASD ($n=34$) were recruited. A psychologist determined group status/eligibility using DSM-IV-TR criteria after review of previous evaluations and parent report of symptomatology on the Social Communication Questionnaire.

Prior to the eye examination, patients' parents provided information regarding patients' gender, race, ethnicity, and communication level (nonverbal, minimally verbal, verbal). Parents indicated whether the patient wore a refractive correction, had ever had an eye examination, and patient's age at the last examination.

The eye examination protocol included tests of visual acuity, refraction, convergence (eye teaming), stereoacuity (depth perception), ocular motility, and ocular health. Tests minimized tactile sensitivity issues and incorporated visual, sensory, and communication supports. All patients were examined according to the protocol. Patients' refractive findings and habitual spectacle correction were compared to standardized criteria. Patients with significant differences were retested after wearing new spectacle prescription for one month. Chi-square, Wilcoxon Rank Sum test, and

ANCOVA were used to compare results for the TD and ASD groups.

Results:

TD and ASD groups did not differ by age (p-value 0.54), gender (p-value 0.53), or ethnicity (p-value 0.22). ASD patients were less likely to be corrected for refractive error (44% compared to 15%, $p=0.014$). Binocular visual acuity after wearing appropriate correction was poorer for ASD patients ($p=0.006$). ASD patients were more likely to show reduced convergence on near point of convergence (48% compared to 7%, $p<0.001$) and positive fusional vergence testing (39% compared to 15%, $p=0.042$). Stereoacuity was poorer in ASD patients ($p<0.0001$). Ocular motility accuracy was reduced in ASD patients. Testability was generally high (TD 100%; ASD 88-97%), except for intraocular pressure (IOP) measurement. IOP testability was significantly reduced for ASD patients (71 % compared to 89 %) ($p= 0.083$) and varied with communication level ($p< 0.001$); 37.5 % for nonverbal, 44.4 % for minimally verbal and 100 % for verbal ASD patients.

Conclusions:

Most patients with ASD can complete vision testing within an eye examination protocol. Testability of intraocular pressures is reduced, particularly for nonverbal and minimally verbal patients. Patients with ASD are more likely to have significant uncorrected refractive error, poorer corrected binocular visual acuity, reduced convergence, and less accurate eye movements. Future research is needed to refine examination procedures and investigate treatment implementation in this population.

162.118 118 Overcoming Barriers to Intervention in Behaviorally-Based Treatments for Sleep Disorders. K. S. D'Eramo* and M. J. Palmieri, *The Center for Children with Special Needs*

Background: The development of effective and sustainable interventions for behavioral sleep disorders among individuals with ASD is critical. Research suggests the prevalence of sleep problems among the ASD population may reach 83%. Studies show numerous consequences of

disrupted sleep including behavioral dysregulation, irritability, impaired executive functioning, health problems, obesity, increased accidental injury, and long-term risk for psychiatric problems. The assessment and treatment of sleep disorders among individuals with ASD requires a systems approach and is largely a caregiver training model. Clinicians depend on caregivers residing with the child to provide accurate data for evidence-based assessment, to actively participate in treatment planning and implementation, and to follow procedures designed to promote sustainability beyond the termination of formal treatment. Beyond the obstacles associated with training parents, there may be other individuals who contribute to treatment implementation but are not directly involved with the treating clinician.

Objectives: In this paper we describe the process of systems navigation in the treatment of sleep disorders with an emphasis on strategies to address obstacles related to evidence-based assessment (e.g., developing reliable data collection systems), intervention development (e.g., collaborative selection of evidence-based treatment approaches the caregiver finds feasible to implement), training (e.g., training caregivers to successfully train babysitters and extended family members), and movement from treatment to sustainability (e.g., managing regression).

Methods: All data presented in the paper are collected from patients presenting to a Behavioral Sleep Clinic for individuals with ASD. All patients treated in the Sleep Clinic first undergo a comprehensive assessment which includes parent completion of the Albany Sleep Problems Scale, submission of a minimum of 14 nights of baseline data on sleep habits and behavioral patterns, and a thorough developmental history. Throughout intervention parents collect daily data on sleep and behavioral patterns and following the assessment, data are collected at scheduled intervals.

Results: Data from families treated in the sleep clinic illustrate the ways in which barriers to treatment are identified and addressed. Overall, results across patients support an increase in time spent sleeping independently and decrease in time spent engaging in problem behaviors at bedtime during active treatment, with gains

sustained for up to three years post-intervention. Examination of individual data patterns reveals periods in which bedtime problem behaviors increase and/or time spent in independent sleep decreases. These data patterns are meaningful and relevant to treatment as they are indicative of barriers to intervention. Examples from patients at various points in the treatment process will be used to illustrate such barriers, including barriers associated with data collection systems, treatment integrity challenges associated with inconsistent implementation across multiple caregivers, challenges associated with generalization to new locations, and management of regression at 36-month post-treatment follow-up.

Conclusions: Sustainable improvements in sleep habits require an approach to intervention that is guided by ongoing evidence-based services. A highly collaborative approach in which the caregiver is well engaged in the development of data collection systems, intervention selection, and ongoing data review is crucial to success. When such a model is adopted, sustainable change can be achieved.

162.119 119 Lack of Evidence of Effect of Risperidone On Core Autistic Symptoms Over Years of Time: Analysis of Data From a Longitudinal Study. H. M. Underwood, Y. Zhang, N. Marrus and J. N. Constantino*, *Washington University School of Medicine*

Background:

Risperidone is FDA-approved for the treatment of irritability in children with Autism Spectrum Disorders (ASD). Previously-published short-term treatment studies have suggested beneficial effects for core ASD symptoms.

Objectives:

This study capitalized on a life-course longitudinal study of children with ASD to examine the effect of risperidone on the course of core ASD symptoms over time.

Methods:

Parents of 200 children in the Washington University Sibling Study provided retrospective summaries of the interventions received by their ASD-affected children over the course of their

clinical care. Yearly parent-report assessments using the Social Responsiveness Scale (SRS) were conducted over the course of the longitudinal study. Parents of 51 of the children reported that the child had received a trial of risperidone. Twenty-eight had at least two SRS assessments related to the course of risperidone treatment: 19 had baseline SRS assessments documented prior to initiation of treatment and at least one SRS assessment following initiation of treatment; 9 had no available baseline assessment but at least two SRS assessments recorded following initiation of risperidone treatment. Parents of 23 of the children reported that their children were improved on risperidone (mean age 6.4, SD 3.3; mean duration of treatment 52.8 months, SD 33.7). Parents of the other 5 subjects indicated that risperidone was ineffective or associated with unacceptable adverse effects (mean age 6.7, SD 3.7; mean duration of treatment 69.4, SD 32.2). Intra class correlation for serial assessments on the SRS during the course of risperidone treatment (i.e. test-retest reliability for the sample as a whole) was 0.91, $p < 0.00001$.

Results:

Among children whose parents reported that risperidone treatment was sustained because it was beneficial, the mean change in total SRS score from baseline (prior to initiation of medication) to the latest available follow-up during the period of use was an increase of 14.9 points on total SRS score (SD 18.2). For children with more than one SRS report while on risperidone ($n=19$) the mean rate of change in SRS score during risperidone treatment was an increase of 3.4 points per year. There was no association of time-rated change in score with either age or severity of autistic impairment at the time of the earliest available SRS assessment. There were no significant time-rated improvements in any of the SRS sub scales. Parents' narrative reports of improvement in their children related to reduced aggression, better attention, less anxiety, fewer mood swings, and better task focus. For the children whose parents reported a negative effect from treatment risperidone, SRS scores remained unchanged or worsened over the course of treatment.

Conclusions:

In this naturalistic longitudinal study, children affected by ASD whose parents reported benefit from long-term use of risperidone did not show evidence of improvement in core autistic symptomatology over time. Given cumulative risks of long-term use of atypical neuroleptics, these results underscore the importance of periodic re-evaluation of the magnitude of medication effect for children with ASD receiving neuroleptic treatment.

162.120 120 The Effectiveness of a Robot-Intervention Compared to a Human-Trainer Intervention in Promoting Question Asking in Children with Autism Spectrum Disorders. B. Huskens* and R. Verschuur, *Dr. Leo Kannerhuis*

Background: Recent studies targeting self-initiated question asking have shown that children with Autism Spectrum Disorders (ASD) are able to engage in self-initiated question asking, and that self-initiated question asking can be generalized to the home situation. Recently, technology is becoming increasingly important in interventions for children with ASD, for example by using speech generating devices during communication interventions, computer games or robots. Until now the studies investigating the effectiveness of robot-interventions are only exploratory and have methodological limitations. Drawing firm conclusions is therefore difficult.

Objectives: The aim of the present study was to promote self-initiated question asking in school-aged children with ASD by conducting a robot-intervention and a human trainer-intervention. The objective was to investigate the effectiveness of both interventions.

Methods: Data were collected using a combined crossover multiple baseline design across participants. Six children were randomly assigned to two experimental groups. During the sessions a statement-question-action scenario was used to elicit self-initiated questions. During the intervention, using a least-to-most prompting hierarchy, the children were prompted either by the robot or the human trainer to initiate a question related to a statement. Data-analysis involved visual inspection and the calculation of Tau_{novlap} that examines data nonoverlap between phases. The overall Tau_{novlap} was also calculated.

Results: The results revealed that the number of self-initiated questions significantly increased

between baseline and the first intervention for both experimental groups. The values of Tau_{novlap} showed a significant increase for all children. The number of self-initiated questions remained high during the subsequent phases of the study.

Conclusions: Both the robot-intervention and the human trainer-intervention effectively promoted self-initiated question asking in children with ASD. The high number of self-initiated questions during follow-up indicates that both experimental groups maintained this skill. Practical implications and directions for future research will be discussed.

162.121 121 The Use of Humanoid Robots As Co-Therapists in ABA Therapy for Children with Autism Spectrum Disorder. J. J. Diehl*¹, C. R. Crowell¹, M. Villano¹, K. G. Wier², K. Tang¹, M. Van Ness¹, J. Flores¹, T. Freeman¹, E. A. Klinepeter¹, S. Matthews¹, S. L. Mazur¹ and N. M. Shea³, (1)*University of Notre Dame*, (2)*Logan Center*, (3)*Syracuse University*

Background: Recent technological advances have opened the possibility of using robots as co-therapists in behavior therapy for individuals with Autism Spectrum Disorder (ASD), but most research has focused on technology development rather than clinical applications. The goal of this project was to examine a clinical approach to the use of a robot co-therapist in Applied Behavior Analysis (ABA) therapy for children with ASD.

Objectives: We had two specific aims: (1) to examine whether a robot co-therapist enhances outcomes for children with ASD compared to standard approaches involving only a human therapist, and (2) to examine whether in-session improvements can be generalized to natural environments.

Methods: Participants were 19 individuals with ASD between the ages of 6-13 years with varying levels of cognitive and language ability. Diagnoses were confirmed using the ADOS, SCQ-Lifetime, and clinical judgment. Participants completed 12 ABA therapy sessions as well as a baseline and posttest session. In six of the 12 sessions, the participant received therapy with a human therapist and a robot co-therapist, and from a human therapist only in the other six sessions. Order of presentation (robot + therapist first or therapist only first) was counterbalanced within matched pairs. Each session consisted of 30 to 40 minutes of ABA therapy administered by

a social skills coach trained by a licensed psychologist and board certified behavior analyst with extensive experience working with individuals with ASD. In this study, we used the NAO platform (Aldebaran Robotics) as our robot co-therapist and controlled it with the DOMER program (Villano et al., 2011), a graphical user interface that allows a person to wirelessly control a NAO during a session. Using DOMER, the robot was controlled remotely by an unseen person, who observed the session and selected appropriate social responses for the robot. Measurements included in-session behavioral tracking, psychophysiological responses of the child as measured by an Affectiva Q Sensor, natural environment behavioral tracking sheets completed by the parents at several time points, and baseline/posttest evaluations of behavior using a number of parent report measures.

Results: Overall, between baseline and posttest, participants showed a decrease in social skills deficits, $t(18)=2.07$, $p<.05$, as measured by the Autism Social Skills Profile, and a trend toward a decrease in repetitive behaviors, $t(18)=1.72$, $p<.10$, as measured by the Bodfish Repetitive Behaviors Scale – Revised. While in-session behavioral tracking and electrophysiological responses showed considerable variability in performance, participants showed a marked increase in the frequency of parent-recorded targeted behaviors in their natural environment between baseline and posttest, $t(17)=2.79$, $p<.01$. Many participants showed greater improvement in targeted behaviors during sessions involving the robot, although this difference did not reach significance.

Conclusions: Overall, we found improvements in targeted behaviors and these gains generalized to natural environments, although it is important to note that there was considerable variability in behavioral and electrophysiological responses to the robot. It will be important to understand the factors that might contribute to this variability, and also to determine the ecological validity of this approach.

Background: Young children with a diagnosis 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 intervention delivered early appears to have a beneficial effect on outcome. These three issues come together in the promising application of novel technologies to social difficulties of very young children.

Objectives: The Click-East research project aims to investigate whether it is possible to teach the fundamentals of social attention to pre-schoolers with autism through a specially designed iPad app.

Methods: The app has been developed using a participatory design process with children with ASD, parents, teachers, and other professionals. A series of pilot tests formally explored the responses of children and parents to the app, and to working with an iPad more generally. The completed app is now being evaluated in a rigorously designed randomised controlled trial ($n=60$) with immediate and delayed intervention groups, membership stratified by autism severity. Evaluations at time one include the *Mullen Scales of Early Learning*, the *Autism Diagnostic Observation Schedule*, a parent-child free play session, and background questionnaire data. There is follow-up immediately after a two month intervention period and again at 6 month follow-up. The primary outcome measure will be the ADOS-C (ADOS-change) to look for differences in social and communicative behaviour during parent-child interaction.

Results: Participatory design and pilot data demonstrate that the app is motivating, user-friendly and practical in a family setting. Eleven families in the immediate intervention group have now completed the intervention period, producing an average of 8 hours and 40 minutes game play, or 8.5 minutes per day. Parent report measures indicate a very high level of satisfaction with the intervention and evidence of motivated and enthusiastic engagement with the app by the participating children. There is anecdotal evidence

of generalized skill development including learning new vocabulary and improvements in single-finger pointing. Additionally, many families use the iPad as a reward for positive behaviour. By IMFAR 2013 we will be able to present equivalent post-intervention data from the full sample of 30 families in the immediate intervention group, including data collected within the app and associated parent-report and behavioural measures.

Conclusions: The early signs are that this new technology holds great potential for work with children with autism. We will consider our findings in the light of pragmatic approaches to education and support: technological solutions can be delivered quickly and cheaply and provide spin-off benefits for families (e.g. peer respect, increased on-task behaviour). In this context, the intervention may be worthwhile even if therapeutic outcomes are relatively modest. We hope to go on to develop a suite of apps for children with ASDs across a range of ages and ability levels, and are actively seeking industry partners to support this work

162.123 123 Neurobehavioral Changes After Web-Based Socio-Emotional Remediation in Autism, 22q11.2 Deletion Syndrome, and Developmental Delay. B. Glaser*, *University of Geneva Medical School*

Background:

The current study tests *VisAVis*, a non-commercial web-based software program designed for children and adolescents (ages 7-16) with mild retardation. *VisAVis* targets working memory, emotion recognition, and focusing on the eyes of the face: core weaknesses in both autism and 22q11.2 deletion syndrome (22q11DS). While much is known about the impact of impaired face processing on emotion recognition and social skills, there is a paucity of tools that can be used to teach faces and emotions to school-age children. We designed *VisAVis* to target socio-emotional deficits and cerebral hypoactivation in individuals with autism (ASD) and 22q11DS.

Objectives:

To evaluate whether the *VisAVis* program contributes to changes in reasoning, facial

emotion recognition, behavior, and BOLD response during functional MRI.

Methods:

Nineteen (high and low functioning) previously diagnosed participants with ASD and 16 participants with 22q11.2 deletion syndrome were compared with 14 individuals with developmental delay (all aged 7-16). All participants completed the twelve-week *VisAVis* program and underwent cognitive-behavioral evaluations and functional MRI at pre-remediation (preR), post-remediation (postR), and 12 weeks post-remediation (post-rest).

Results:

The autistic and 22q11DS groups showed marked improvement in nonverbal reasoning (measured by the Raven Matrices) after remediation at postR and post-rest (preR < postR & post-rest: $F(2, 88)=3.467, p=.037$), and recognition of facial emotional expressions at postR and post-rest (preR < postR & post-rest: $F(2, 88)=107.768, p<.001$). We also observed decreased problem behaviors (total and internalizing as measured by the CBCL) at postR in all groups (total: $F(2, 86)=4.102, p=.028$); internalizing: $F(2, 86)=4.866, p=.014$). During a block design task comprised of photos from multiple visual categories, functional imaging analyses showed increased BOLD response in the fusiform gyrus to faces in ASD at postR and in the superior temporal gyrus at postR and post-rest for the 22q11DS group.

Conclusions:

To our knowledge, *VisAVis* is the first software program to be piloted and subsequently studied using standardized behavioral and neuroimaging measures in multiple diagnostic groups. Our findings support *VisAVis* as a tool for working on socio-emotional impairments in ASD and 22q11DS during middle childhood, and bolster previous studies showing changes in BOLD response in the fusiform gyrus after teaching individuals with ASD to focus on the eyes of the face.

162.124 124 Effects of Video-Based Group Instruction On Generalized Social Behavior of Adolescents with Severe Autism. M. C. MacFarland* and J. B. Plavnick, *Michigan State University*

Background: Numerous strategies for teaching social skills to individuals with autism have emerged in the intervention literature. Despite some practices with efficacy for teaching targeted behaviors, there is minimal evidence documenting generalization of social behavior to novel settings following social skills interventions for individuals with autism. Plavnick, Sam, Hume, & Odom (in press) recently piloted and assessed a version of a social skills group procedure that included video modeling and several strategies known to promote generalization including multiple exemplar training, programming common stimuli, and general case programming (Stokes & Baer, 1977). The intervention, video-based group instruction (VGI), led to the acquisition of complex social behavior and parents reported the generalization of targeted skills, though generalization was not assessed through direct observation of behavior. Additional research focused on generalization of skills following exposure to VGI is needed to better understand the efficacy of this procedure.

Objectives: The purpose of the present investigation was to evaluate the extent to which social initiations and responses taught during VGI sessions generalize to novel settings. A secondary purpose was to identify additional components, if necessary, that mediate generalization of social behavior following VGI.

Methods: A single-case experimental research design was used to identify a functional relation between VGI and generalization of social behavior by 11 adolescents diagnosed with autism and a severe cognitive impairment. A multiple baseline across groups design was used to evaluate the efficacy of VGI to promote generalization of social initiations and responses. Participants were observed in multiple settings across a public school prior to and following implementation of VGI, which was administered only in the classroom environment, to observe instances of generalization.

Results: Preliminary data suggests some generalization of social responding, though variability across participants has been observed.

Individuals with more severe deficits in language and social behavior prior to the intervention were less likely to engage in generalized social behavior following the intervention. Additional strategies, including training across multiple environments and peer mediated interventions, were needed to facilitate generalization of social behavior for all participants. Educational service providers and parents reported increased instances of social behavior, suggesting that VGI may promote generalization of social skills for individuals with autism.

Conclusions: The results of the study show that VGI may be a strategy capable of teaching social behavior to adolescents with autism and promote generalization of social skills in untrained settings. The findings extend previous research in several ways. First, the present experiment was designed to explicitly assess generalization of social behavior rather than evaluating generalization as a secondary purpose. Second, the intervention involved adolescents diagnosed with autism and who demonstrated a severe cognitive impairment. Minimal research has included such participants to date. Finally, the intervention was delivered in a public school environment and incorporated into the daily curriculum of participants. These extensions have several implications for future researchers and practitioners that will be discussed.

162.125 125 Effects of Video Modeling Interventions On Social and Communication Skills of Children with Autism Spectrum Disorders: A Meta-Analysis. C. Qi*, Y. L. Lin and M. Collier, *University of New Mexico*

Background:

Research has provided evidence of the effectiveness of video modeling (VM) interventions on social skills for individuals with autism spectrum disorders (ASD; Shukla-Mehta, Miller, & Callahan, 2010). Researchers have reached agreement on using meta-analysis in synthesizing single-case designs studies as it can result in more objective evaluation of multiple studies (Van den Noortgate & Onghena, 2003). Statistical procedures have been developed to provide more rigorous evaluations of the effectiveness of the intervention for single-case studies than traditional methods such as visual analysis.

Objectives:

The purpose of the study was to examine (1) the effectiveness of VM on social and communication skills of young children with ASD, (2) the relative effectiveness of VM in comparison to VM plus additional strategies, (3) the effectiveness of different models used in VM (self vs. others), and (4) the effects of potential moderators (child age, gender, or setting) on the effectiveness of VM on the outcomes. Four single-case research metrics were computed: the percentage of non-overlapping data (PND), the percentage of data points exceeding the median (PEM), the pairwise data overlap squared (PDO²), and the robust improvement rate difference (IRD).

Methods:

Inclusion criteria were that studies must (a) be published in English language, peer-reviewed journals between 1985 and 2011, (b) include at least one participant with ASD aged from 2-8 years, (c) utilize a single-case design that demonstrated experimental control, (d) have a baseline with at least three data points, (e) include a graphic display of child outcomes, (f) use VM only or VM with additional components, and (g) utilize outcome measures that targeted on social and communication skills as the primary dependent variables.

Results:

Twenty-six studies with 59 effect sizes were included for the meta-analysis. We adopted the criteria set by Scruggs and Mastropieri (1998) to categorize effects using the PND: a PND more than 0.90 is considered as very effective intervention, 0.70 to 0.89 as effective, and less than 0.70 as questionable or ineffective. We used these criteria to evaluate all the PND, PEM and PDO² methods. We used the Park et al. (2009) criteria to categorize effects using the IRD: an IRD more than .50 is considered an effective intervention and less than .50 ineffective. The mean values of PND (.73), PEM (.82) and PDO² (.85) obtained for 59 participants across studies all indicated that VM was considered an effective intervention for improving social communication skills of young children with ASD. The mean IRD values of .72 suggested a 72% improvement rate from baseline to intervention phrases. Child gender, age, and intervention settings, VM types (VM only vs. VM plus additional strategies), and

model types (other vs. self) were not related to the outcomes of the study.

Conclusions:

All four metrics calculations indicate that VM intervention is effective to increase social and communication skills of children with ASD. However, findings should be interpreted with caution because of the limitations of using percentage of nonoverlapping data.

162.126 126 Self-Regulation of Amygdala Activation by Unhappy Emotion Using Real-Time fMRI Neurofeedback with Autistic Spectrum Disorder -a Pilot Study-. T. Saito*¹, T. Haji², T. Ito², T. Matsuda² and Y. Okubo¹, (1)*Nippon Medical School*, (2)*Tamagawa University*

Background: Functional magnetic resonance imaging (fMRI) has revolutionized the study of the human brain. It was realized that as the fMRI technique has advanced the on-line processing of data would offer the possibility for immediate quality assurance of data and make real time fMRI (RtfMRI) data processing possible. RtfMRI enables a completely new type of experiment, whose designs and stimuli can adapt on-line to the participants' measured brain activity. Neurofeedback is a specific form of biofeedback, which feeds back information about brain activity to allow for training of voluntary regulation of brain activity. In this neurofeedback experiments using RtfMRI participants learn to control brain activity by contingent feedback of measures of the brain activity. In recent years, neurofeedback using RtfMRI applications have gained significant interest enabling potential clinical applications. It would allow us ask questions such as what areas are accessible to neurofeedback, how self-regulation is mediated, how self-regulation can be learned, what kind of behavioral effects can be induced and how specific they would be. This study addresses the potential clinical application of neurofeedback using RtfMTI for autistic spectrum disorder (ASD) in order to learn how to regulate their emotion.

Objectives: The current study investigates whether RtfMRI is a useful method for ASD patients to learn how to regulate unhappy emotion.

Methods: The ASD subjects (mean age: 18.6 years-old) were enrolled in the study and had independent clinical diagnosis of Asperger's disorder according to DSM-IV-TR. At first subjects were trained to down-regulate brain areas responsive to unhappy emotions evoked by showing unhappy pictures. A target area was identified by the contrast between responses to unhappy and neutral pictures in a localizer scan to ensure that an area involved in unhappy emotion processing was selected. In the localizer scan, we assessed brain responses to unhappy and neutral pictures by presenting a set of pictures of the same emotion category. We used pictures from the IAPS. After subjects were trained with a set of pictures, subjects were instructed to downregulate the brain area responsive to words such as "unhappy" and "neutral" in stead of the pictures. For the neurofeedback, a continuous signal from the target area was displayed using the picture of a thermometer whose dial indicated the amplitude of the fMRI signal in the target area. Changes in the amplitude were indicated as the percent of signal change. Patients were not given any specific instructions about strategy. We acquired fMRI data on a 3 Tesla Siemens Trio-Tim.

Results: Subjects were able to decrease activation in amygdala during downgulation periods of the neurofeedback scans. Analysis of the contrast between conditions with word "unhappy" and "neutral" in the localizer scans yielded activation in the MPFC/insula. This indicate decreased activation in amygdala with nuerofeedback might be associated with MPFC/insula.

Conclusions: The pilot study shows ASD subjects were able to regulate amygdala activity and neurofeedback using RtfMRI for ASD has potential usefulness. Further studies are required to confirm the effectiveness of neurofeedback using RtfMRI for ASD.

Cognition and Behavior Program

163 Infant Cognition and Behavior

163.127 127 Maternal Communicative Style in Interaction with Infant Siblings of Children with ASD. J. Quigley* and S. McNally, *Trinity College Dublin*

Background:

Functional aspects of infant-directed-speech (IDS) play a central role in infant development (Venuti,

de Falco, Esposito, Zaninelli & Bornstein, 2012) and are important in shaping infant responsiveness (Goldstein, King & West, 2003), yet only a few studies have examined this with mothers of heightened-risk-for-autism (HR) infants (e.g., Jakubowski & Iverson, 2011; Meirsschaut, Warren & Roeyers, 2011). Further, there is little consensus on associated infant outcomes, in particular in the case of ASD. For example, Landry & Bryson (2004) showed that frequent redirection and solicitation rather than following of infant attention involves a shifting of attention that is difficult for children with ASD but Kasari, Gulsrud, Freeman, Paparella & Helleman (2012) found that directing the child's attention had long-term beneficial effects on language development in autistic preschoolers.

Objectives:

- To investigate maternal functional speech styles in interaction with HR infants;
- To analyse the relationship between maternal functional style and infants' cognitive, language and socio-communicative development.

Methods:

16 English-speaking mothers (low/middle-SES) and their 17 infants participated: ten infants with no known developmental risk factors, without an autistic sibling and with no family history of ASD (low-risk LR, 7 m; 3 f) and seven HR infants, defined as having at least one older sibling(s) with a clinical diagnosis of ASD (2 m; 5 f, incl. monozygotic twin girls). Dyads were filmed in face-to-face interaction every four weeks over a period of months leading up to their first birthday (mean infant age in months at first visit: 3;7 LR, 5;2 HR). All maternal vocalisations coded into four mutually exclusive categories (regulatory; attention-solicitation; question; responsive-contingent) were calculated as a proportion of mothers' total output. Infants were administered the BSID-III and ESCS at 12 and 18 months.

Results:

Only proportions of responsive utterances contingent upon infant behaviour were significant, where mothers of low-risk infants (Mdn=0.18)

were significantly more likely than mothers of high-risk infants ($Mdn=0.13$) to produce responsive speech ($U=14$, $p<.05$). Attention-solicitations were a more prominent feature of the HR mothers' speech relative to the LR group but not significantly so.

Significant associations with maternal IDS and infant test scores were found for the LR dyads only: responsive speech was positively associated with infants' overall language outcomes at 12 months (Kendalls tau- $b=.71$, $p<.01$) and with Receptive Language Subscale scores (Kendalls tau- $b=.58$, $p<.05$). Attention-solicitations were significantly and negatively associated with both language outcomes at 12 (Kendalls tau- $b=-.61$, $p<.05$) and 18 months (Kendalls tau- $b=-.63$, $p<.05$) and with cognitive outcomes aged 18 months (Kendalls tau- $b=-.62$, $p<.05$).

Conclusions:

The lower rate of responsive-contingent utterances to the HR infants may be because the infants are less active and provide less opportunity for maternal commentary and response (they had lower IJA scores as measured by the ESCS than the LR infants, see also Mahdhaoui et al., 2011 & Wan et al., 2012). The increased incidence of attention-solicitations to HR infants does not appear to have the detrimental effect on developmental outcomes evidenced for the LR infants and may have a place in intervention and training programmes.

163.128 128 The Emergence of Imitation From 9 to 12 Months in Younger Siblings of Children with Autistic Spectrum Disorders: Preliminary Findings From a Longitudinal Study. A. Boudreau^{*1}, I. M. Smith², J. M. Keans¹, J. A. Brian³, S. E. Bryson⁴, N. Garon⁵, W. Roberts⁶, C. Roncadin⁷, P. Szatmari⁸ and L. Zwaigenbaum⁹, (1)*Dalhousie University*, (2)*Dalhousie/TWK Health Centre*, (3)*Holland Bloorview/ Sick Kids*, (4)*Dalhousie University/TWK Health Centre*, (5)*Mount Allison University*, (6)*University of Toronto*, (7)*Peel Children's Centre*, (8)*Offord Centre for Child Studies & McMaster University*, (9)*University of Alberta*

Background: Imitation deficits are well documented in autistic spectrum disorders (ASD; Rogers & Williams, 2006). Indeed, imitation deficits are among the predictors of ASD by as early as 12 months of age (Zwaigenbaum et al., 2005) and accuracy of early imitation is reduced in infants at risk for ASD (Young et al., 2011).

However, little is known about the atypical, versus typical *emergence* of imitation over time. Few studies examined qualitative differences in pre-imitative behavior (approximations to imitation, Kaye & Marcus, 1981; Nichols, 2005). Moreover, no infant sibling study has examined emerging imitation during the critical developmental period between 9 to 12 months.

Objectives: (1) To replicate a hierarchy of precursors of imitation in low-risk (LR) controls. (2) To extend the findings to a high-risk (HR) infant sibling sample, compared with LR controls. (3) To examine imitation differences in diagnostic groups (HR/LR) from 9 to 12 months.

Methods: HR and LR participants were evaluated at 9 and 12 months of age using the imitation task from the Autism Observation Scale for Infants (AOSI; Bryson et al., 2008). The AOSI is a semi-structured play schedule that measures early signs of ASD. The examiner presented the infant with 3 actions (oral-facial movements or actions with objects) and 1 to 3 trials per action, depending on the infant's successful performance. Video records of AOSI administrations were coded using Noldus Observer software and a novel detailed coding scheme. Imitation was scored in 3 ways: (1) total imitation, (2) best score across actions, and (3) approximations to imitation (predictable hierarchical patterns of behavioral responses to the model; e.g., touching model's hands after model claps).

Results: We compared infants' imitation scores (i.e., total imitation, best score and approximations to imitation) using 2 (age) by 3 (diagnosis) mixed repeated measure ANOVAs. Infants were grouped according to 36-month outcome as: (1) siblings *with* ASD (ASD siblings); (2) siblings *without* ASD (non-ASD siblings); and (3) low-risk controls (LR). Preliminary results from the first 31 infants coded ($n's = 10$ ASD siblings, 10 non-ASD siblings, 11 LR) replicated a hierarchy of 'approximations to imitation' in the LR group. Further, ASD siblings demonstrated fewer self-directed approximations than the LR controls. As expected, imitation performance increased with age [$F(1, 28) = 8.79$, $p = .006$]. A main effect of diagnostic group [$F(2, 28) = 3.45$, $p = .046$] revealed that ASD siblings imitated less frequently than did the non-ASD siblings and LR. There was no group by age interaction.

Conclusions: The study provides initial evidence supporting the use of a hierarchy of approximations to imitation as an approach to studying the atypical emergence of imitation skills. Preliminary findings suggest HR-ASD siblings differ from non-ASD siblings and LR controls both in frequency of fully imitative acts and in quality/level of approximations to imitation. These differences are evident by age 9 months and remain at 12 months. The results may have implications for understanding psychological mechanisms underlying the emergence of imitation deficits, and for early detection and intervention in ASD.

163.129 129 Ethical Issues Related to Research On Siblings. B. Siegel*, *University of California, San Francisco*

Background: Having a child with an autism spectrum disorder (ASD) is a major life stressor. These stressors have clear reciprocal antecedents between the child with ASD and his/her parents. In addition, typically developing siblings also are impinged by the autism-related stressors of their parents, as well as by the maladaptive symptoms of their affected siblings. There is relatively sparse empirical literature on psychosocial outcomes in adults siblings, though it has been found that the unaffected siblings' gender and birth order have some predictive validity with respect to adult family role relationships. Less amenable to empirical study have been ethical issues raised when examining the culture of families living with autism and rearing both affected and unaffected siblings together.

Objectives: Research & Diagnostic Issues: 1) When and how to couch a discussion of possible ASD or broader autism phenotype (BAP) in an incidentally-observed young sib? What are the ethical challenges in infant sib research, i.e., early sensitization to risk for ASD in a child who develops completely typically? 2) How to accomplish research on affected pedigrees without over-representing recurrence data such that it may lead to stoppage (birth of further children) despite actual etiologies that may be epigenetic or due to de novo mutations? 3) In the future, when parents can know whether a fetus will develop some form of autism, will parents have any moral obligation to unaffected sibs as they decide whether or not to have an affected child?

Parent Issues: 1) Is the sibling being conceived of, and born to be a role model when young, and/or 'brother's keeper' when an adult? 2) If becoming one's brother's keeper is made an explicit expectation to adult sibs, what is that sib's moral and ethical obligation to fulfill this role? 3) Are siblings conferred moral obligation to be a helper to affected sib (the 'There but for the grace of God go I' conundrum)?

Sibling Issues: (Inter-personal) 1) What effect is there on moral development if an unaffected sib's sense of 'right' forms around dual behavior standards for him/herself and for his/her affected sib? 2) (Intra-personal) How can/should therapists help unaffected sibs struggling with antipathy to a sib with ASD, or with disentanglement from an enmeshed family system resolve these issues so as to pursue his/her own life goals?

Methods: These issues will be explicated, and qualitatively illustrated by narrative responses to these questions provided by siblings of adults with autism 21-26 years old being followed in a prospective study by the author and colleagues.

Results: Adult siblings run the gamut from those physically detached and struggling to be productive, attributing difficulties to their family of origin to those altruistically pursuing graduate careers (e.g., from neuroscience to design of residential communities for adults) as a result of their rearing experiences.

Conclusions: These, as well as 'intermediate' outcomes that siblings link to their rearing will be discussed in the context of siblings' birth order, gender, and degree of disability in their sibling.

163.130 130 Temperament in Infants At Heightened Risk for Autism. B. M. Winder*¹, A. Wahed¹, L. Rescorla¹ and S. Paterson², (1)*Bryn Mawr College*, (2)*The Children's Hospital of Philadelphia*

Background:

Much recent research effort has been put toward identifying early behavioral manifestations of a later ASD diagnosis. Temperament is a potential early sign of ASD because it is viewed as being inherited or at least constitutional in nature, evident early in life, and stable across

development. The few studies that have examined temperament as an early indicator of ASD have used parent report only.

Objectives:

The goal of this "baby sib" study was to compare infants who later received an ASD diagnosis (HR-D infants) with infants at no known risk for developing ASD (LR infants) using a parent-report measure as well as an observational measure of temperament.

Methods:

Temperamental variables were coded using the *Minnesota Preschool Affect Rating Scales* (MN-PARS; McPhee & Shapiro, 2004), while parent report was collected using the *Infant Behavior Questionnaire - Revised* (IBQ-R; Gartstein & Rothbart, 2003). These measures were collected at the 6- and 12-month time points for 31 infants at heightened risk for ASD (HR-D = 8) and 15 age-matched LR infants. The Child Behavior Checklist/1½ to 5 (CBCL; Achenbach & Rescorla, 2000) was collected at 24 months. Autism diagnostic status was determined at 24 months by trained clinicians.

Results:

LR infants displayed more negative affect at 6 months and less negative affect at 12 months than HR-D infants, who showed the opposite pattern, as indicated by significant and large the age x group interaction for MN-PARS Negative Affect was, $F(1, 21) = 5.37, p = .031, h_p^2 = .20$. On IBQ Negative Affectivity, HR-D infants displayed significantly more negative affect at 12 ($t = -2.193, df = 20, p = .040$) but not 6 months ($t = .277, df = 21, ns$) than LR infants. Although many significant correlations were found within each temperament measure, there were virtually no significant correlations between IBQ-R temperament dimensions and conceptually similar MN-PARS ratings at 6 or 12 months. Qualitative inspection of MN-PARS temperament profiles suggested that 6 months HR-D infants appeared more passive and dull than the LR infants with a switch at 12 months towards more irritability and less adaptability. The measure that best differentiated the HR-D and LR infants was the

Pervasive Developmental Problems Scale on the CBCL/1½ to 5, which was administered at 24 months.

Conclusions:

While the agreement between the measures was not found at 6 and 12 months, some insights on the early temperament of infants at heightened risk for ASD were revealed. In particular, negative affect emerged as an area of temperamental interest and qualitative temperamental profiles emerged that suggest a change in temperament from 6 to 12 months for the infants who later receive a diagnosis.

163.132 Interactions Between Gaze Following and Disengagement At 7 and 13 Months in Infants At High Risk for Autism Spectrum Disorder. R. Bedford*¹, T. Gliga², M. Elsabbagh³, A. Pickles¹, J. Fernandes⁴, A. Senju², T. Charman⁵, M. H. Johnson² and .. The BASIS Team⁶, (1)Institute of Psychiatry, (2)Birkbeck, University of London, (3)Centre for Brain and Cognitive Development, (4)Birkbeck, University of London, UK, (5)Institute of Education, (6)BASIS

Background: Emerging findings from high-risk studies suggest that infants who develop autism spectrum disorder (ASD) show early impairments in the processing of both social and non-social stimuli (Bedford et al., 2012; Zwaigenbaum et al., 2005). Although ASD is defined by social-communication impairments and restricted and repetitive behaviours, the majority of cognitive theories of ASD posit a single underlying factor, which over development has knock-on effects across domains. In order to examine the developmental interactions between measures of social and non-social attention, we looked at the relationship between gaze following and visual disengagement across the first year of life.

Objectives: In this study concurrent and longitudinal links between gaze following behaviours and disengagement were examined in low-risk controls and high-risk infants at two time points, 7 and 13 months. We aimed to test 1) whether these abilities are independent and remain separate from early on in development; or 2) whether they become separate over time.

Methods: Participants were 54 infants at high risk for ASD and 50 low-risk controls recruited through the British Autism Study of Infant Siblings

(BASIS). In the gaze following task, Tobii eye-tracking was used to record gaze behaviour. Infants were shown 12 short videos of a female model turning to look at one of two objects. Infants' proportion of congruent versus incongruent first looks and their looking time to the congruent object were calculated. In the gap-overlap task a central stimulus was presented to gain the infants' attention followed by the onset of a peripheral stimulus either at the same time as the central one disappeared (baseline) or while the central stimulus was still on the screen (overlap). Data were video coded and disengagement was calculated as reaction time in overlap – baseline trials.

Results: An autoregressive cross-lagged model was run on the whole sample and provided a good fit to the data. At 7 months there was a significant relationship between disengagement and both measures of gaze following behaviour, first look and looking time. Faster disengagement in the gap-overlap task predicted increased looking to the congruent object, but a higher proportion of incongruent (versus congruent) first looks. No significant longitudinal relationships between the measures were found from 7 to 13 months nor was there a concurrent relationship between the measures at 13 months. The majority of children who later developed ASD at 3 years showed impairments in either gaze following or disengagement at 13 months, with only a small proportion of children having difficulties with both abilities.

Conclusions: This study finds that attentional disengagement is related to gaze following behaviours early on in development, at 7 months, with a possible speed/accuracy trade-off, in which faster disengagement gives the infant more time to look at the target object, but leading to an increase in orienting errors. By 13 months, the age at which these measures relate independently to ASD outcome, they have become de-correlated, perhaps suggesting that the neural regions subserving these behaviours follow different patterns of specialisation across development (Johnson, 2001).

163.133 133 Tonic and Phasic Saccadic Reaction Time Differences in Infants At High Risk for ASD. E. J. Jones^{*1}, S. Wass¹, T. Charman², M. H. Johnson¹ and *. the BASIS Team¹,
(1)*Birkbeck, University of London*, (2)*Institute of Education*

Background:

Visual attention is the primary means of environmental exploration for young infants. Orienting to stimuli is a key component of visual attention that has been linked to the development of self-regulation (e.g. Posner & Rothbart, 1998), and early atypicalities in visual orienting may therefore have pervasive effects on later development. Studies of visual orienting in high-risk infants have revealed that such atypicalities may be a risk factor for the development of autism (Elsabbagh et al., submitted; Zwaigenbaum et al., 2005). This work has traditionally examined mean reaction times derived from a series of trials. However, recent work has shown that examining intra-individual variability can provide additional insight into mean-based effects (Milne et al., 2011; Dinstein et al., 2012). To further characterize visual orienting atypicalities in the early development of autism, in this study we explored intra-individual variability across an attention-shifting paradigm in infants with older siblings with autism.

Objectives:

To examine within-task variability in attention-shifting in 7- and 14-month-old infants at familial high-risk for autism.

Methods:

Participants were infants with older siblings with autism ('high-risk'; n=53) or typical development ('low-risk'; n=27). At 8- and 14-months, infants completed the gap-overlap task, a computer-based test of visual attention shifting. Current analyses focused on latency to saccade measured in two conditions: Gap, in which the central stimulus disappears 200ms before peripheral stimulus onset; and Baseline, in which the central stimulus disappears simultaneously with peripheral stimulus onset. We examined i) mean reaction times; ii) intra-individual variability using ex-Gaussian modelling; iii) change in performance across the four blocks of the task.

Results:

1. Mean comparisons: Mean baseline saccadic reaction times were significantly

faster in high-risk than low-risk infants at 8 but not 14 months; mean saccadic reaction times in gap trials did not significantly differ by risk group at either age.

2. Intra-individual variability: Ex-Gaussian modeling of individual reaction times indicated that the reaction-time distribution had a longer tail in the low-risk group; there were more trials with reaction times >1200ms in the low-risk group at both 8 and 14 months.
3. Changes with time: At both 8m and 14m, group differences in baseline RTs were most pronounced in the last block of the paradigm. At 14m, this was driven by slower reaction times in the second vs first half of the paradigm in low-risk but not high-risk infants. In gap trials administered later in the paradigm, at 14m high-risk infants produced greater numbers of very rapid (<200ms) saccades than low-risk infants.

Conclusions:

High-risk infants showed shorter overall saccadic reaction times to the appearance of stimuli in non-competition conditions and fewer prolonged reaction times associated with 'zoning out' at both 8 and 14m; and at 14m in later blocks showed no slowing of baseline reaction times and more very rapid saccades in the gap condition. This pattern of findings is consistent with the suggestion that high-risk infants maintain a heightened vigilance to their environment. Talk 3 will present further data consistent with this proposal.

163.134 134 Fixation Durations During Static Scene Viewing in 6-8-Month-Old High-Risk Infants Relates to ADOS Scores At 36 Months. S. Wass^{*1}, T. Gliga², E. J. Jones², T. Charman³ and M. H. Johnson², (1)University of Cambridge, (2)Birkbeck, University of London, (3)Institute of Education

Background: Research into the early development of attention in Autism Spectrum Disorders (ASD) has mainly used experimental paradigms such as the gap-overlap task. However, it how remains poorly understood how differences in reaction time latencies on these tasks relate to altered behaviour in more naturalistic contexts, where previous research has suggested that contrasts between ASD and typical

development may be most acute (e.g. Speer et al., 2007).

Here, we report a series of analyses that looked at spontaneous fixational eye movement behaviours during the unconstrained viewing of a static scene. These analyses offer a method for bridging the gap between experimental and more naturalistic assessments of attention.

Objectives: To investigate spontaneous fixational eye movement behaviours in the early development of ASD.

Methods: We measured spontaneous fixational eye movement patterns during viewing of a static scene consisting of a mixture of faces and non-social objects in 6-month-old infants, 45 of whom were at high familial risk of developing ASD (HR) and 47 at low familial risk (LR) (cohort 1). Viewing data was recorded at 50/60Hz using a Tobii 1750/T120 eyetracker. We administered an identical test to an independent cohort of 40 HR and 43 LR infants aged 8 months (cohort 2). Cohort 1 was followed up for outcome characterisation at 36 months, using the Autism Diagnostic Observation Schedule (ADOS).

Analysis of fixational eye movement behaviours was performed using previously published Matlab scripts (Wass et al., 2012). Fixations were identified as periods in which the eye remains static (defined as a period of >100ms with no change in reported position of gaze >35 degrees per second during that period).

Results: For cohort 1, we found that HR infants showed significantly shorter fixation durations than LR infants, even when possible confounds such as number of usable fixations and eyetracker data quality were accounted for. An identical analysis conducted on data from cohort 2 found the same group difference. Between-group differences in fixational eye movements were found to be consistent across fixations targeted at social and at non-social objects.

We found that shorter fixation durations at 6 months related to higher Autism Diagnostic Observation Scores scores at 36 months, after confounding variables were controlled for.

Comparison of results from the gap-overlap task showed a significant correlation between shorter fixation duration and faster saccadic orienting times in the baseline (non-competition) condition.

Conclusions: These results are consistent with the results from Talk 2, in which faster reaction times under non-competition conditions were identified in HR vs LR infants. The findings suggest that abnormalities can be identified in spontaneous attentional orienting behaviours in ASD during the first year of life.

One possible explanation for these findings is increased vigilance, modulated by short-term changes in arousal (cf e.g. Aston-Jones et al., 1981; de Barbaro et al., 2012).

163.135 135 Better Visual Search in Infants At Risk for ASD. T. Gliga^{*1}, R. Bedford², T. Charman³ and M. H. Johnson¹,
(1)*Birkbeck, University of London*, (2)*Institute of Psychiatry*,
(3)*Institute of Education*

Background: Superior attention to details has frequently been described as a characteristic of ASD (Happé, 1999) and has been explained in terms of a diminished bias to attend to global structures or the semantic content of visual scenes (Happé & Frith, 2006). More recently it has become clear that superior perceptual abilities are not only measured in a situation of competition between local and global information processing. For example, children and toddlers with ASD were shown to be faster at detecting targets in visual search tasks (O’Riordan et al, 2001; Kaldy et al. 2011). However, these abilities may still be only a consequence of underdeveloped abilities to process or attend to higher-level information rather than their cause.

Objectives: To investigate visual search abilities during the first year of life in children at-risk for ASD (owing to having an older sibling with this disorder). We want to determine whether superior visual search is measurable before a bias to attend to attend to global versus local information is established.

Methods: Twenty-five low-risk participants (LR) and 35 high-risk participants (HR) took part in an eye-tracking (Tobii) study at 8 and 14 months of age. Participants saw circular displays of 1 target

and 7 distractors, all letters (app. 9° from the centre of the screen). Targets were either visually Similar to the distractors (a “V” or “+” target was presented together with 7 “X” distractors) or Dissimilar (an “S” or an “O”). Stimuli were presented for 1.5 seconds. We measured the percentage of trials in which a fixation on a target was made. At 24 months we measured the ability to integrate local information into a global percept, by measuring recognition of textured silhouettes.

Results: At 8 months only an effect of Trial type was observed, participants performing better in the Dissimilar target condition. At 14 months the high-risk group performed better than the low-risk group for both Trial types (no significant interaction between Group and Target type). The ten highest scores belonged to HR infants. Number of fixations before reaching the target and fixation duration on the target will also be analysed, as well as the relationship between visual search abilities and silhouette recognition.

Conclusions: Better visual search (measured as a greater proportion of trials with target fixations) was observed in high-risk infants at 14 months of age. This replicates findings in toddlers with ASD (Kaldy et al, 2011) and extends those findings by demonstrating an earlier onset of perceptual differences. This is consistent with perceptual differences preceding and possibly driving later difficulties with global-level information processing (Happé, 2012). The lack of a differential effect of Trial type suggests that HR are not necessarily better at discriminating targets from distractors but that they are more willing to orient to these odd-one-out stimuli. This is in line with previous talks in this symposium showing faster orienting in high-risk infants.

163.136 136 Risk-Markers of Autism Spectrum Disorder in a Cohort of Newborn Infants. T. Farroni^{*} and V. Di Gangi, *University of Padua*

Background:

Recent publications have shown behavioral differences from 6 to 9 months between siblings of older children with ASD (high risk-HR) and siblings of children with typical development (low risk-LR) (see Elsabbagh et al. 2009, 2012; Ozonoff et al., 2008 for a review). Previous works have demonstrated that children with autism have

deficits in attentional (dis-)engagement mechanisms (gap effect, Van der Geest et al., 2001) and in processing of social information, particularly faces (Dawson, 2005). Furthermore, young children with autism can differentially process direct and averted gaze when viewing faces (Grice et al., 2006).

Objectives:

The aim is testing newborns to detect the earliest developmental atypicalities that may be associated with autism or the broader autism phenotype (BAP). We compare at low and at high risk newborns by using behavioral marker tasks, designed to assess attention to social and non-social stimuli; offering some support to previous behavioral studies with older individuals with ASD, and suggesting the presence of social attention processing abnormalities very early in the development.

Methods:

Attentional tasks are tested at birth in both groups (HR and LR) using the following established paradigms: the "gap effect" task with face-like stimuli (Farroni et al., 1999) and the "eye contact" task (Farroni et al., 2002) with faces showing direct and averted gaze. Eight 2 to 5-day-old newborn infants (siblings of an individual with ASD) have been tested so far, using the gap-overlap experimental paradigm and a spontaneous preference between mutual and averted gaze. The first task measures the "cost" of disengaging from a central stimulus in order to fixate a peripheral target. This task measures the latency of orienting towards peripheral cues depending on the temporal gap between a central stimulus and the peripheral target and depending, in the case of newborns, on the kind of peripheral target (upright vs inverted face). A second task tests the ability to discriminate between direct and averted gaze as demonstrated in previous studies.

Results:

From the behavioral pattern in both experiments emerges a remarkable variability on attentional and visual responses in the HR sample compared with the LR sample. ASD-sibling newborns have

shown atypical patterns in engagement and disengagement behavior in both tasks. The HR group shows a lack of the typical gap effect and in particular is slower to orient when a face appears in the periphery. In the case of eye contact task the HR group shows the same trend as the LR group (preference for direct gaze) but they have a lower number of orientation towards direct gaze with a very lower fixation time during the exploration of the stimuli.

Conclusions:

Our results confirm the possibility of identifying early behavioral risk-markers. A longitudinal design could make more clear the developmental trajectory of these abilities and the connection with the ASD attentional phenotype, in order to timely categorize possible predictors of the core deficits in autism.

163.137 137 Markovian Dynamics of Visual Scanning Behavior in Toddlers with ASD. G. Ramsay*¹, D. Lin², W. Jones¹ and A. Klin¹, (1)Marcus Autism Center, Children's Healthcare of Atlanta & Emory University School of Medicine, (2)Harvard-MIT Division of Health Sciences and Technology

Background: Research has shown that children with autism exhibit atypical patterns of visual attention to social scenes relative to typically developing peers. In previous studies involving presentation of audiovisual stimuli comprising faces and shapes synchronized to varying degrees with speech and tones, we showed that ASD infants are relatively insensitive to social contingencies afforded by talking faces, focusing instead on physical contingencies in the form of audiovisual synchrony between light and sound. Viewing patterns of TD/DD controls indicated a preference for synchronous faces and speech, lacking in ASD participants, even though TD/DD/ASD groups did not differ in baseline sensitivity to audiovisual synchrony. In those studies, measures of visual fixation were derived from summary statistics comparing mean fixation durations on different parts of the screen. These measures do not capture patterns of temporal correlation in the eyetracking trajectories, which may contain information about behavioral responses specific to autism.

Objectives: Accordingly, the goal of this research is to develop a mathematical model for parameterizing the full spatiotemporal dynamics

of visual scanning behavior, and to determine whether temporal dynamics distinguish ASD from TD children.

Methods: Drawing on our research developing stochastic models of goal-directed actions, we constructed a hidden Markov process to model our data. In our model, looking patterns are characterized by a Markov chain comprising a finite-state grammar of discrete events modeling the intention to look at regions of interest within a scene, with state-dependent duration distributions modeling event timing. Probability distributions of spatial targets associated with each state model the shape of those regions. A linear system models oculomotor dynamics, smoothing out each random sequence of spatial targets. Eyetracking trajectories are modeled by transforming the state space into screen coordinates. Using the Expectation-Maximization Algorithm, we derived maximum-likelihood estimates that allow us to recover the parameters of the Markov transition kernel from training data. We also derived optimal nonlinear smoothing algorithms that enable the hidden states of the model to be estimated for any given eyetracking trajectory. Finally, we derived likelihood-ratio tests to determine which of a set of trained models is most consistent with any observed test set of eyetracking trajectories. The result is a complete system for automatically quantifying, interpreting, and classifying the full spatiotemporal dynamics of visual scanning behavior. We applied the model to eyetracking data for 20 ASD and 20 TD toddlers from previous experiments using preferential looking paradigms to assess sensitivity to audiovisual synchrony. We trained models for each diagnostic group and stimulus type, and tested for significant differences in each of the model parameters.

Results: We found differences in Markov parameters across diagnostic groups reflecting temporal sequencing and timing of saccades and fixations, which depended on the social nature of the stimulus. These differences cannot show up in our summary statistics.

Conclusions: Significant differences in visual scanning behavior exist between ASD and TD children that cannot be fully quantified without characterizing the detailed temporal unfolding of individual looking patterns, suggesting specific

mechanisms of attention that may be crucial in identifying children at risk of autism.

163.138 138 Measuring Callous-Unemotional Traits in Autism Spectrum Disorders. L. Roughan*¹, D. H. Skuse² and W. Mandy³, (1)*Great Ormond Street Hospital NHS Foundation Trust*, (2)*Institute of Child Health, UCL*, (3)*Faculty of Brain Sciences, UCL*

Background: The presence of callous unemotional traits (CU) has been an important specifier in defining the severity and prognosis of individuals with Conduct Disorder. However, little is known about whether these traits can be reliably measured in individuals with ASD. The potential overlap between the ASD phenotype and children presenting as seemingly callous, unemotional and uncaring may impact on the ability to measure CU traits in this population. The inventory of callous-unemotional traits (ICU) has been widely validated in the general population and is thought to provide an efficient, reliable measure of CU traits in young people. Although research suggests certain deficits seen in ASD (e.g. cognitive perspective taking) are qualitatively different to the deficits seen in CU (e.g. affective empathy deficits), it remains unclear as to whether these qualitative differences between CU traits and ASD can be captured in an informant report questionnaire such as the ICU.

Objectives: To test the extent to which the ICU measures a construct above and beyond ASD trait severity. To identify the proportion of an ASD sample who are regarded as having psychopathic tendencies (as measured by the ICU) in order to inform appropriate cut offs for ICU in an ASD population.

Methods: Cross-sectional data were examined for 56 (87.5% males) young people. A well-standardised parent report interview (3Di) was used to measure ASD. Parent and teacher report SDQ scores for conduct problems were also captured. The Inventory of Callous-unemotional Traits (ICU) parent and teacher scores were used to measure CU traits.

Results: Correlation analysis indicates a relationship between parent reported measures of ASD severity and CU traits (*Social reciprocity* $r = .56$, $df = 55$, $p < .05$; *Communication* $r = .40$, $df = p < .05$; *Repetitive behaviours* $r = .22$, $df = 55$, $p = .11$, ns). However, the relationship between

ASD and teacher reported CU traits is not indicated (*Social reciprocity* $r = .084$, $df = 55$, $p = .54$, ns; *Communication* $r = -.09$, $df = 55$, $p = .50$, ns; *Repetitive behaviours* $r = -.04$, $df = 55$, $p = .79$, ns). The proportion of young people with ASD reported to have CU traits (>33 on ICU) was higher than the general population (Parent report CU = 58.9%; Teacher report CU = 42.9%). CD symptoms were reported in a significantly lower proportion of the sample (Parent report CD = 17.9%; Teacher reported CD = 12.5%).

Conclusions: Using gold-standard CU trait measures in an ASD clinical sample probably leads to a significant over-reporting of CU traits. This could be partially explained by the strong relationship between ASD severity and CU traits, which may reflect conceptual and phenotypic overlap between these two constructs. Cut offs for the ICU need to be modified for an ASD population; and different items may be needed to accurately identify CU traits in the ASD population. Clinicians and researchers should be cautious using the ICU to measure CU traits in ASD populations.

163.139 139 Temperament in Children with Autism Ages 4-7: A Study Using the Inventory of Children's Individual Differences- Short Form. J. M. Campbell¹, B. Barger² and C. A. Simmons³, (1)University of Kentucky, (2)The University of Georgia, (3)University of Georgia

Background: To date, only a handful of studies have investigated the role of temperament in ASD in children and most have relied on instruments designed to measure constructs from either Thomas and Chess or Mary Rothbart's temperament theories. Furthermore, few have investigated gender differences within ASD or ASD status X gender temperament interactions.

Objectives: The purpose of this study is to determine whether temperament variables measured with the new Inventory of Children's Individual Differences- Short Form (ICID) differentiate children with ASD from typical children, as well as determine whether ASD status X gender interactions are present in early childhood.

Methods: Here we report a 2 (ASD versus typical) X 2 (Gender) age controlled MANCOVA comparing 139 children with ASD (113 male; 26 female) and 374 control children (190 male; 187

female) between the ages of 4 and 7 (Early Childhood; EC) on the 15 temperament subscales of the ICID. Data from ASD children was collected on-line via the Interactive Autism Network (IAN) and data from typical children was taken from the norming sample data set provided by Dr. Roy Martin.

Results: Pillai's Trace statistics indicated a trend for significant gender interactions [$F(1, 15) = 1.683$, $p > .05$, $\eta^2 = .06$], significant gender differences [$F(1, 15) = 1.742$, $p < .05$], and significant differences between ASD and typical children: [$F(15,1) = 39.924$, $p < .001$]. Only significant differences in regards diagnosis and interactions are considered here. Follow up Welsch F tests indicated no significant ASD X gender interactions, but diagnostic group differences were reported favoring lower scores for ASD on achievement [$F(1, 438) = 69.42$, $p < .001$], compliance [$F(1, 438) = 81.89$, $p < .001$], consideration [$F(1, 438) = 251.02$, $p < .001$], intelligence [$F(1, 438) = 27.36$, $p < .001$], openness [$F(1, 438) = 27.36$, $p < .001$], positive emotion [$F(1, 438) = 41.12$, $p < .001$], and sociability [$F(1,438) = 346.12$, $p < .001$]; higher scores for the ASD groups were reported on antagonism [$F(1, 438) = 27.66$, $p < .001$], distractible [$F(1, 438) = 63.69$, $p < .001$], fear/insecurity [$F(1, 438) = 35.54$, $p < .001$], negative emotion (anger) [$F(1, 438) = 100.33$, $p < .001$], shy [$F(1, 438) = 286.73$, $p < .001$], and strong willed [$F(1, 438) = 44.52$, $p < .001$]. No differences were found on activity level [$F(1, 438) = 0.61$, $p = .44$] or organized [$F(1, 438) = 7.39$, $p < .01$] and no significant gender X ASD diagnostic status interactions were found.

Conclusions: Collectively, these results indicate widespread temperament differences between children with ASD and typically developing children. Furthermore, no gender X ASD diagnosis interactions were reported. The strongest differences were on the variables of sociability and shyness, temperament traits related to the core diagnostic symptoms of ASD.

*This project is funded by a grant from the Organization for Autism Research

163.140 140 Are Early Neurophysiological Markers of ASD Syndrome-Specific? Preliminary Results From a Cross-Syndrome Study. D. D'Souza¹, H. Kyjokova², M. H.

Johnson¹, T. Gliga¹, E. Kushnerenko³, G. Scerif² and A. Karmiloff-Smith¹, (1)*Birkbeck, University of London*, (2)*University of Oxford*, (3)*University of East London*

Background: ASD is a neurodevelopmental disorder characterised by gross and sustained impairment of social interaction and communication. ASD diagnosis is by behavioural criteria, which do not emerge clearly until age two or three. As a consequence, little research has been done on the very early development of autism. Recent studies have begun to bridge this gap by carrying out prospective studies of younger siblings of children already diagnosed with ASD (*Sibs*). This is an important strategy because one in five *Sibs* goes on to an autism diagnosis. The British Autism Study of Infant Siblings (BASIS) is a large-scale prospective study, a key goal of which is to help clinicians and researchers identify early markers of autism. This will not only contribute to our understanding of ASD, but will also enable earlier, more effective interventions, which could significantly improve subsequent quality of life. Indeed, several early markers are already emerging. However, before a measure can be said to be an early marker of ASD, it is crucial to determine whether it is syndrome-specific.

Objectives: The aim of the present study is to determine whether BASIS measures yield syndrome-specific or syndrome-general findings, by testing infants/toddlers with other genetic syndromes (namely, Down syndrome (DS), fragile X syndrome (FXS), Williams syndrome (WS)) on the same battery of tasks. Here we present preliminary data from one of these tasks, which seek to elucidate the way in which infants/toddlers process changes in speech sounds and pitch.

Methods: Auditory event-related potentials were studied in infants/toddlers with DS (N=27), FXS (N=10), and WS (N=30). Sounds were presented oddball: 70% of the sounds were /u/ vowels (standards), 15% were /u/ vowels with a different pitch to the standards (pitch deviants) and 15% were /i/ vowels with the same pitch as the standards (speech deviants). The data were compared with data from *Sibs* (N=51) and controls (N=22), who had been tested on identical measures.

Results: The infant equivalent of the preattentive mismatch negativity (MMN) in response to pitch deviants was found in all groups except in FXS, reflecting atypical discrimination of pitch in FXS. In response to speech deviants, the MMN occurred 150 ms late in WS (reflecting atypical discrimination). The P3a component (attentive orientation) in response to speech deviants was seriously attenuated in the *Sibs* group, reflecting reduced attention to speech changes. The P3a was found in all other groups.

Conclusions: First, auditory processing was atypical in FXS, WS, and *sibs*. Second, the *Sibs* brain did not attach any importance to changes in speech sounds, whereas the DS, FXS, WS, and typically-developing brains did. These data are preliminary, but they hint at the identification of an early marker of autism, one that occurs as early as 14 months of age and is syndrome-specific.

163.141 141 Early Predictors of Empathy At School Age in Siblings of Children with ASD. T. Hutman*¹ and M. Sigman², (1)*UCLA Center for Autism Research and Treatment*, (2)*University of California, Los Angeles*

Background: Children with ASD attend less and demonstrate less affective response to others' distress (Sigman et al., 1992). Response to distress has been associated with the ability to intuit the internal states of others and with the quality of social interactions. Attenuated distress response has been documented as early as 12 months of age in infants later diagnosed with ASD (Hutman et al., 2010). Infant siblings of children with autism who were not later diagnosed with ASD did not show atypical distress response. However, a subset of 12-month-old infant siblings with non-specific delays did show a significant reduction in attentiveness to distress relative to typically developing controls (Hutman et al., 2012).

Objectives: This study sought to determine whether reduced empathic concern was evident in 5½-year-old siblings of children with ASD. Early characteristics such as joint attention, social attention, response to distress, verbal and non-verbal cognitive skills were evaluated as predictors of individual differences in empathy at 5½ years.

Methods: Participants were 23 children with no family history of autism and 40 children with a sibling diagnosed with autistic disorder (Sibs). When children were 5½, their parents completed a 23-item, Likert-scale measure, characterizing the affective and cognitive components of their child's empathic behavior in a variety of contexts (Griffith Empathy Measure; Dadds et al., 2008). Predictors of empathy that were tested include verbal and non-verbal cognitive skills (Mullen, 1995), response to distress (Sigman et al., 1992), preferential attention to social stimuli (Hutman et al., 2012), and response to an examiner's bids for joint attention (RJA; Early Social Communication Scales; Seibert, Hogan, & Mundy, 1982). Predictive measures were administered when infants were 12 and 18 months old.

Results: Parent ratings of child empathy did not differ between low-risk controls and Sibs who were not themselves diagnosed with ASD ($p's > .6$). However, a subset of high-risk infants who demonstrated developmental delays at 5½ years ($n=12$) received lower cognitive empathy ratings from their parents than high- and low-risk participants who were developing typically ($p=.03$). Delays observed in this group include elevated ADOS scores and impaired language skills. Significant predictors during infancy of individual differences in parent-reported empathy at school entry included attention to an examiner feigning distress at 12 and 18 months ($p's < .01$). Relations were still in evidence when we controlled for ASD symptom severity (Gotham et al., 2009). Parent-reported empathy at 5½ years was not related to affective response to the examiner's distress, RJA, or verbal and non-verbal cognitive skills measured during the second year ($p's \geq .06$).

Conclusions: Impaired empathic response is not consistently evident among 5½- year-old siblings of children with autistic disorder. Parents reported decreased cognitive empathy in a subset of Sibs with developmental delays, but who do not meet criteria for ASD. A similar pattern has been reported in 12-month-old Sibs with developmental delays (Hutman et al., 2012). This study provides support for developmental continuity between distress response at 12 months and parent-reported empathy at 5½ years. Implications for early detection and intervention will be discussed.

163.142 142 Very Early Brainstem Function Together with Attention Regulation Relate to Later ASD in NICU Graduates: Replication and Extension. J. M. Gardner*¹, I. L. Cohen¹, B. Z. Karmel¹, H. T. T. Phan¹, P. M. Kittler¹, S. Parab² and A. Barone², (1)*NYS Institute for Basic Research in Developmental Disabilities*, (2)*Richmond University Medical Center*

Background:

Identifying early indicators for Autism Spectrum Disorders (ASDs) could be useful for screening. We have reported behavioral abnormalities more prevalent in NICU graduates later diagnosed with ASD (Karmel et al, 2010), including visual preferences for higher stimulation rates when less aroused at 4 months post-term-age (PTA), an attention pattern more typical of newborns. Such dysfunction suggests problems in early arousal-modulated-attention (AMA), likely regulated by brainstem processes. We further have reported conjoint association of this abnormal attention regulation with abnormal transmission speeds in auditory brainstem evoked responses (ABRs), also reflecting brainstem dysfunction, predicts increased ASD risk in NICU graduates (Cohen et al, AS 2012). We now report on different samples and relations to later behavioral development.

Objectives:

To ascertain if previous findings: (1) can be replicated in an independent subsequently-diagnosed sample; (2) can be generalized to non-ASD samples at risk for ASD such as younger siblings of ASD children and high-medical-risk NICU infants, and (3) are related to atypical development associated with later-emerging ASD such as neurobehavioral functioning on standardized tests.

Methods:

Medically at-risk infants and infant siblings recruited as newborns for longitudinal follow-up studies were compared. Four groups defined: 1. ASD(Dx1): initial sample, $n = 27$; 2. ASD(Dx2): replication sample, $n=21$; 3. non-ASD(SIB): younger siblings of ASD, $n = 36$; 4. non-ASD(OTHER): remaining NICU cohort, $n=1740$. Groups contrasted on: (1) ABR neural transmission speeds: click ABRs obtained within a

few days after birth (after 32wks post-conception). Abnormality was determined by component peak latencies significantly deviating from age norms at 80dBnHL; ~12Hz for Waves I,III,V and III-V interval, which typically resolved before hospital discharge; (2) Attention regulation: AMA measured at 4 months PTA in paired-comparison design with 2 same checkerboard-patterned stimuli flashing at 1,3, or 8 Hz square-wave modulated frequencies when infants more and less aroused due to feeding and additional stimulation. Slope of the preference function across the 3 stimuli $> .1$ defined looking at higher rates (8Hz $>$ 3Hz $>$ 1Hz); (3) Standardized measures: Bayley Infant Neurobehavioral Screener (BINS), 2½mos; Bayley Scales of Infant Development (BSID), 4-7mos.

Results:

There was a very high incidence of abnormal ABRs related to ASD compared to the overall NICU sample (72% vs. ~28%), with non-ASD(SIB) ~50%. The 2 diagnosed samples did not differ in % abnormal ABRs or any behavioral measures indicating replication and were combined (ASD(DxC)) for analyses. ASD(DxC) showed more looking at higher rates than non-ASD(OTHER). The combined effect of an initial abnormal ABR with AMA slope $> .1$ predicted ASD. 60% of ASD(DxC) had both compared to 17% non-ASD(OTHER) and 0% non-ASD(SIB). Interestingly, non-ASD(SIB) had significantly lower scores on the BINS compared to ASD(DxC) and non-ASD(OTHER), which may represent developmental problems not within criteria for ASD, although no differences on BSID were apparent at these young ages and small sample sizes.

Conclusions:

Dysfunction during early brainstem development indicated by altered neuronal transmission speeds, along with deficits in attention regulation as early as 4 months of age, may represent a potentially important path leading to later ASD not apparent through standardized tests during early infancy.

Background: Impaired disengagement of attention is the earliest attentional deficit reported in infants at high-risk for autism (HRA) and may be associated with a later diagnosis of the autism spectrum disorder (ASD). Efficient disengagement of attention plays a significant role in the development of both joint attention and arousal regulation. Therefore, early deficits in attentional disengagement may result in the atypical development of both of these processes and contribute to the emergence of the heterogeneous ASD phenotype.

Objectives: To investigate the association between attentional disengagement, measured at 6-months, and development of joint attention, novelty processing, and arousal modulation (measured at 12 and 18 months) in HRA and low-risk comparison (LRC) infants.

Methods: HRA and LRC infants completed visits at 6, 9, 12, and 18 months of age. An eye-tracking paradigm was used to assess the efficiency of attentional disengagement at 6 months ($n = 24$ HRA; $n = 20$ LRC). Latency to disengage attention was measured as the time necessary to shift attention from a central fixation (i.e., a face) to a peripheral target. Joint attention abilities were assessed using observational measures: the Communication and Symbolic Behavior Scales (CSBS) and the Autism Observation Scales for Infants (AOSI) at 12 months, and the Autism Diagnostic Observation Schedule (ADOS) at 18 months. Arousal regulation was measured using a series of parent questionnaires: the Infant Behavior Questionnaire (IBQ) at 12 months, Toddler Behavior Assessment Questionnaire (TBAQ) at 18 months, and Infant Toddler Social Emotional Assessment (ITSEA) at 12 and 18 months. Items and subscales for these measures were standardized and averaged to create joint attention and arousal regulation composite variables at 12 and 18 months.

Results: Latency to disengage attention at 6 months was not significantly different for HRA and LRC groups. For the LRC group, but not the HRA group, faster disengagement latency was associated with better joint attention skills at 12, $r(17) = .56, p < .05$, and 18, $r(18) = .44, p < .1$,

months. For the HRA group, slower attentional disengagement was related to poorer arousal regulation at 12 months, $r(20) = .70, p < .01$.

Conclusions: Efficient disengagement results in the adaptive allocation of attention (e.g., sharing attention with a communicative partner; joint attention) and facilitates early arousal regulation. Preliminary results suggest that faster attentional disengagement is associated with more skillful joint attention abilities at 12 and 18 months in LRC but not HRA infants. In contrast, for the HRA group, increased latency to disengage attention was associated with greater aversion to novelty. Although preliminary, our findings suggest that atypical attentional disengagement may have sequelae that, in combination with other primary disturbances, result in the heterogeneous phenotypic end-state associated with ASD.

163.144 144 Dissociating Content-Influenced Changes From Maturational Changes in Oculomotor Function in Infants with Autism Spectrum Disorders. T. Tsang*, W. Jones and A. Klin, *Marcus Autism Center, Children's Healthcare of Atlanta & Emory University School of Medicine*

Background: Research regarding vision in autism spectrum disorders (ASD) has produced two separate bodies of literature related to oculomotor function—one using traditional saccade-eliciting paradigms (e.g. gap/overlap task), another using natural viewing paradigms. Together, they suggest that basic mechanisms of oculomotor function appear to be largely intact in autism, but that content- and context-dependent attentional biases offer evidence of distinct differences between individuals with ASD and their typically-developing (TD) peers. Previous research has provided converging evidence that individuals with ASD attend preferentially to non-social aspects of the environment. However, it remains unclear when, developmentally, this bias emerges, and whether it is due to motivational factors that guide attention or to developmental changes in response to physical factors that capture attention. The present study will chart basic oculomotor response while viewing naturalistic as well as abstract stimuli during the first two years of life, in order to shed light on how both exogenous and endogenous attentional systems affect visual behaviors in infants who develop ASD.

Objectives: The current study will chart the longitudinal development of visual fixation responses and saccadic eye movements during natural viewing of social scenes and during prosaccades to peripheral targets, and will compare these changes in infants who develop ASD and their TD peers.

Methods: Fixation and saccades were identified from data in a longitudinal study using eye-tracking equipment to examine the viewing patterns of naturalistic scenes in infants at high and low risk for developing ASD. Eye-tracking data were collected at 2, 3, 4, 5, 6, 9, 12, 15, 18, and 24 months while infants viewed videos of actresses engaging in child-directed caregiving behaviors, toddlers interacting with each other in playground settings, and geometric animations. Diagnoses were given at 36 months, assigning infants into ASD ($n=13$) and TD groups ($n=51$). The following properties and content of eye movements were analyzed cross-sectionally and longitudinally, and then compared between groups: fixation duration; frequencies of saccade and fixations; saccade latency and accuracy; relationship between saccade amplitude and duration; and relationship between saccade velocity and amplitude.

Results: Preliminary analyses suggest that while basic properties of saccades and fixations undergo developmental change, they do not differ between infants with ASD and their TD peers. Moreover, there are clear indicators that saccadic properties for both groups are influenced by content, demonstrating the emergence of endogenous control of saccades in early infancy. However, these groups differed in when and where they looked. Infants with ASD did not show difficulty disengaging but were more likely to saccade between non-social aspects of the scene.

Conclusions: Basic oculomotor circuitry appears to develop normally in individuals with ASD. Properties of eye movements reflected task-specific differences. This suggests that discrepancies in viewing patterns between toddlers with ASD and their TD peers are not the result of oculomotor impairments, but rather reflect differences in what aspects of a social scene are most salient to them. Our data provide converging evidence pointing to top-down rather

than low-level visual factors influencing dynamic visual engagement between these two groups.

163.145 145 The Ability to Integrate Audiovisual Speech At 8 Months of Age Is Associated with Later Receptive Language. E. Kushnerenko^{*1}, H. Ribeiro², T. Gliga², P. Tomalski³, T. Charman⁴ and M. H. Johnson², (1)*University of East London*, (2)*Birkbeck, University of London*, (3)*University of Warsaw*, (4)*Institute of Education*

Background:

Deficits in crossmodal integration might play a role in language and social difficulties in children with ASD (Mongillo et al., 2008). Integration of audiovisual speech information is often investigated with a McGurk paradigm, where conflicting auditory and visual inputs are presented (McGurk & MacDonald, 1976). Although the results are not always consistent across McGurk studies with ASD children, our recent study has demonstrated that infants at low risk for ASD looked longer to the incongruent audio-video displays, while the looking behaviour of infants at high-risk (with an older sibling with autism) did not differ between congruent and incongruent displays, suggesting difficulties in matching auditory and visual information (Guiraud et al., 2012). Little is known about whether audiovisual integration during infancy is consequential for vocabulary growth.

Objectives:

To investigate whether the ability to match audiovisual information at 8-months is associated with later vocabulary development as assessed by Communicative Development Inventory (CDI), in infants at low and high risk for ASD.

Methods:

Twenty-four low risk participants (LR) and 64 high-risk (HR) participants took part in an eye-tracking study at 8 months. At a follow-up visit at 14 months parents of 23 LR and 42 HR infants filled in the Communicative Development Inventories (Oxford-CDI). At 8 months the stimuli were presented in two preferential looking tasks: Mismatch condition with an auditory /ba/ presented with congruent lips movement on one side of the screen and lips mouthing /ga/ on the other side of the screen and Fusion condition with

an auditory /ga/ presented with articulation of /ga/ on one side of the screen (congruent face) and articulation of /ba/ on the other side of the screen (incongruent face). The total fixation length was calculated off-line for each infant for areas of interest around mouth or eyes or the whole face oval using the Tobii Studio software package.

Results:

At the age of 8 months, low-risk infants tended to look longer than high-risk infants at the audiovisually mismatched face (11.2 s vs 9.53 s, $p=0.06$) and mouth (7.9s vs 6.3s, $p=0.08$). At 14 months, LR infants had significantly higher CDI receptive vocabulary than HR infants ($p=0.026$). Looking time to the incongruent mouth in the mismatch condition, as a percentage of looking time to both faces in this condition, correlated significantly with CDI receptive vocabulary at the age of 14 months ($r=0.264$, $p=0.034$).

Conclusions:

As reported previously, audiovisual mismatch condition and fusion condition are processed differently by infants and this ability matures in the second half of the first year of life (Tomalski et al., 2012). The present data demonstrate that at the age of 8 months the ability to integrate auditory and visual speech information might be predictive of later language outcome. This data is in line with the recent reports showing that attention to mouth might be indicative of subsequent language development (Kushnerenko et al., 2012; Young, Merin, Rogers, & Ozonoff, 2009).

*The BASIS Team: S. Baron-Cohen⁵, P. Bolton⁶, K. Davies², M. Elsabbagh⁷, J. Fernandes¹, J. Guiraud², K. Hudry⁴, G. Pasco⁴, L. Tucker²

⁵University of Cambridge, ⁶Institute of Psychiatry, ⁷McGill University

Cognition and Behavior Program

164 Cognition and Behavior III

164.146 146 A Meta-Analysis Examining the Academic Achievement of Individuals with ASD in Reading, Writing and Mathematics. H. M. Brown^{*1}, J. Oram Cardy², L. M.

Archibald², A. Johnson¹ and J. Volden³, (1)Western University, (2)Western University, Canada, (3)University of Alberta

Background: Media reports and popular opinion often portray individuals with ASD either as academically impaired or perpetuate the stereotype of 'autistic genius'. Unfortunately, little empirical research examines the academic profile of individuals with ASD. One notable exception was a research synthesis by Schaeffe-Whitby & Richmond-Mancil (2009) where the results were somewhat mixed. On one hand, they report that individuals with ASD have deficits in comprehension, written expression, and problem solving, yet they also state that their reading, math and writing skills are commensurate with IQ. The current meta-analysis of all studies examining academic achievement between 1990 and the present will clarify whether there is one academic profile for individuals with ASD, the size of strengths or weaknesses across domains and the consistency of these differences.

Objectives: 1. To use meta-analysis to determine the size, direction, and consistency of differences between academic achievement scores and PIQ, among individuals with ASD. 2. To explore whether the effect sizes within each of five academic areas (writing, reading comprehension, decoding, math computation, and math reasoning) are heterogeneous. 3. To describe the predicted range within which their academic abilities vary (across each of the five areas) for individuals with ASD.

Methods: We conducted five meta-analyses of 8 to 18 studies of individuals with ASD that included one or more measures per academic area. Standardized mean differences (SMDs) between the academic achievement scores and PIQ scores were calculated using a random effects model and Hedge's g SMD. The statistical significance of the grand SMD for each academic area was tested with a Z-test, and a Q-test was used to determine whether there was heterogeneity in effects. The range of the population SMD was estimated using the tau-squared method.

Results:

1. The models revealed that academic skills of individuals with ASD were commensurate with PIQ

for decoding and math reasoning. While there were reliable deficits between PIQ and reading comprehension ($g = -0.4$), math computation ($g = -0.4$) and writing ($g = -0.6$), they have little clinical significance.

2. The differences between academic ability and PIQ were heterogeneous suggesting that the overall finding that academic skill does not differ significantly from PIQ is unlikely true for all individuals or groups of individuals with ASD.

3. The range within which the difference between PIQ and academic achievement varied was within $\pm 1SD$ for most of the skills studied. However, the range was generally negatively skewed meaning that a larger proportion of individuals with ASD had weaker skills than predicted by PIQ as opposed to stronger than expected ability.

Conclusions: Academic achievement scores for individuals with ASD vary within the normal range for most of the skills studied. However, with the exception of decoding ability, individuals with ASD were more likely to have difficulties mastering the academic skill than to excel in a given area, and the area of greatest concern was written expression. These meta-analyses support previous findings that the most defining feature of ASD is variability, and that ASD is not associated with any particular academic profile.

164.147 147 ARE Patterns of Aberrant Behaviors Associated to Developmental Trajectories of Adolescents with Autism Spectrum Disorders (ASD) ?. C. Rattaz*, C. Michelon, C. Baeza-Velasco and A. Baghdadli, *Autism Resources Center, CHRU Montpellier and Laboratory Epsilon*

Background:

Challenging behaviors are a critical issue for individuals with Autism Spectrum Disorders (ASD) and their proxy, with a negative impact on their quality of life and outcome. They are related to several clinical characteristics, such as intellectual disability, speech deficits or autism severity (Baghdadli et al, 2008; Matson & Nebel-Schwam, 2007), and may be particularly severe during adolescence. These data are part of the EpiTED cohort, a 10-year follow-up of 152 children with ASD from childhood to adolescence.

Objectives:

The aim of this study was to identify aberrant behavior patterns in adolescents with Autism Spectrum Disorders and to examine if these patterns were associated to their developmental trajectories.

Methods:

Aberrant behaviors were assessed using 4 behavioral domains of the Aberrant Behavior Checklist or ABC (Aman et al, 1985): (I) irritability / aggressiveness, (II) lethargy / withdrawal, (III) stereotypy / self-injury, (IV) hyperactivity / lack of cooperation. Scores are reduced to a scale of 100 in order to make comparisons between domains. The adolescents' developmental trajectories were described using Vineland communication and socialization scores changes over a ten year follow-up (Baghdadli et al, 2012).

Results:

Median scores of aberrant behaviors in the four domains were highly correlated and there was an important heterogeneity among adolescents: (I) irritability = 15.6 (IntQ: 6.7-37.8), (II) lethargy = 25 (IntQ: 14.6-37.5), (III) stereotypy = 23.8 (IntQ: 9.5-42.9), (IV) hyperactivity = 22.9 (IntQ: 8.3-41.7). A cluster analysis allowed us to identify four patterns of aberrant behaviors: a) low score in the ABC four domains, b) high score in irritability and hyperactivity, c) mean score in the four domains and d) very high score in stereotypy, high score in withdrawal and hyperactivity. These four patterns were significantly linked to the adolescents' developmental trajectories, $p < .01$. Most adolescents with a high trajectory (87%) were found in clusters a) and c), whereas adolescents with a low trajectory were equally distributed in the four clusters.

Conclusions:

Those results suggest that, if a high trajectory seems associated with a low level of aberrant behaviors, low trajectory is not necessarily associated with a high level of aberrant behaviors. The impact of an early treatment of behavioral problems for improving individuals with ASD's quality of life and outcome is discussed.

164.148 148 Age Related Changes in Conjunctive Visual Search Among Children with and without ASD. K. Armstrong* and G. Iarocci, *Simon Fraser University*

Background: There is evidence of enhanced visual search performance in people with ASD including toddlers (Kaldy et al. 2011), school age children (O'Riordan et al., 2001), and adults (O'Riordan, 2004). However, previous studies are limited by small sample sizes, using fewer trials than are typically used for visual search tasks and calculating reaction times (RT) based on means instead of medians (McDonald, 2010).

Objectives: The objective of this study was to investigate age related changes in conjunctive visual search performance in a large sample of high functioning children and adolescents with ASD as compared to their age and IQ matched TD peers.

Methods: Participants were between the ages of 7-20 years, and consisted of an ASD (n=49) and a TD (n=42) group. Participants with ASD were high functioning (IQ >80), and matched on IQ and age with the TD group. A conjunctive visual search task was employed; the goal was to find the target (a red 'X') in a multi-element display with red 'T' and green 'X' distracters. It included two blocks of 60 trials (120 total) with two crossed factors: display size (5, 15, 25) and probe (target present or absent). Participants were instructed to press the 'z' key if the target was present, and the '.' key if it was absent.

Results: Analyses were conducted on median RTs of each participant at each display size. A repeated-measures ANOVA was conducted with a between-subject factor of group, and within-subject factors of target presence and set size. Contrary to expectations, there was no difference between the ASD and TD groups on either error or RT (all $p > .05$). The groups were analyzed separately using correlations, with Bonferroni correction. Slope was calculated for each participant using their median RT for each set size, and intercept was calculated using the x-intercept resulting from the slope calculation. Slope is a measure of efficient search strategy and intercept is a measure of processing speed. Age was significantly related to RT performance (measured by the intercept) in both the target present and absent conditions in both groups

($p < .01$); in both groups as participants got older they got significantly faster. Age was not related to slope in target absent or present condition. IQ was not related to any of the performance measures in either group.

Conclusions: Contrary to previous studies, we did not find any differences in performance on a conjunctive visual search task. This may be because this study included a much larger, more heterogeneous sample of individuals with ASD than previously reported studies. We found that similar factors contributed to visual search performance in both groups. Specifically, both groups showed *faster* search performance with age yet their search *strategy* did not change with age. The findings indicate that conjunctive visual search strategy and speed develop similarly in individuals with and without ASD and whereas visual search strategy is mature at age 7 years, the efficiency of search continues to improve until age 20 years.

164.149 149 Age Related Differences of Executive Functions in Children and Adolescents in the Autism Spectrum. S. van den Bergh*¹, A. M. Scheeren², S. Begeer³, H. M. Koot² and H. M. Geurts⁴, (1)*Dr. Leo Kannerhuis*, (2)*VU University*, (3)*VU University Amsterdam*, (4)*University of Amsterdam*

Background: There is a convincing amount of evidence of executive dysfunctions in children and adolescents with Autism Spectrum Disorders (ASD). However, given that patterns of individual profiles of executive functioning (EF) depend partly on age, it is important to take developmental perspective when studying EF in ASD. In everyday life, EF seems clearly deficient in people with ASD, even when adult level performances on EF laboratory tasks are reached. The behavior rating inventory of executive function (BRIEF: Gioia et al., 2000) is widely used in clinical practice to measure everyday EF, but the development of everyday EF in people with ASD has not yet received much attention.

Objectives: Exploring 1) age related patterns in everyday EF of children and adolescents with ASD; 2) the role of symptom severity in these age related patterns; 3) how many children with ASD actually have clinically relevant EF problems in daily life.

Methods: In a cross-sectional study of 116 children and adolescents (15 girls, 101 boys; age

$M = 13$, $SD = 2.8$; age range 6-17) with ASD, four age groups (6-8, 9-11, 12-14, and 15 to 17 years) were compared on four BRIEF subscale scores (inhibition, working memory, shift, and planning). The Autism Diagnostic Observation Scale (ADOS: Lord et al., 2000) severity score was used as ASD symptom severity measure.

Results: For two BRIEF subscales, inhibition, and planning there was a significant effect for age group. Compared to 6-8 year olds, 15-17 years old showed a decrease in inhibition problems, while the other posthoc group comparisons were not significant. Compared to 9-11 year olds, 12-14 year olds showed an increase of planning problems, but again the other comparisons were not significant. There were no significant correlations between symptom severity and the four subscales. Clinical scores of cognitive flexibility were observed in 52% of the sample, and in 44% for inhibition, 25 % for working memory, and 21% for planning. Hence, there are large individual differences in the deficits the children and adolescents with ASD encountered according to their parents.

Conclusions: Consistent with former studies, everyday EF deficits and individual differences were found in children and adolescents with ASD. Positive age development was seen for inhibition, while problems in planning increased with age. This might suggest that age effects for planning are due to changing demands from the school environment. This raises questions whether the BRIEF planning subscale is appropriate to provide information about EF development. Severity did not affect everyday EF. Cognitive flexibility seems to be the main problem area while planning was only affected in a relatively small proportion of the children and adolescents with ASD.

164.150 150 Analysis of Gestural Production During Mother-Child Interaction in Children with Autism Spectrum Disorders, Down Syndrome and Typical Development. M. Mastrogiuseppe*¹, O. Capirci², S. Cova¹ and P. Venuti¹, (1)*University of Trento*, (2)*National Research Council of Italy (CNR)*

Background:

Gestures are a specific type of communicative actions with an important role in intersubjective understanding. Through gestures children take an active part in communication, being able to "tell

without saying" (Capirci et al., 1996). Also children with atypical development, in particular with Down Syndrome use many gestures, particularly to compensate for their verbal impairments (Stefanini et al., 2007). The opposite path is present in children with Autism Spectrum Disorders (ASD) who exhibit deficits in their spontaneous use of gestures (Rapin, 2006). Despite the obvious importance of this issue for children with ASD, literature on gestures in this population is relatively small and is focused on their quantity rather than on their quality. Gestures, moreover, are studied in structured rather than naturalistic contexts. The study of gestures in ASD might give many insights on the construction of communicative intentionality, help identifying different phenotypes and possibly specific therapeutic approaches.

Objectives:

Aim of the present study is to analyze gestural communication in spontaneous interaction between children with ASD and their mothers, focusing on the identification of different types of gestures and on the quality of their execution.

Methods:

60 mother-child interactions were analyzed: 20 children with typical development (TD group; CA: M=24,7, SD=4,1; MA: M=24,7, SD=4,1), 20 with Down Syndrome (DS group; CA: M=40,9, SD=6,3; MA: M=22,5, SD=3) and 20 with ASD (ASD group; CA: M=47,6, SD=11,1; MA: M=25,6, SD=8,9), matched on mental age. Videos were analyzed with a specific coding scheme (Capirci et al., 2007) allowing a quantitative and qualitative analysis of gestural production: gesture function, associated gaze, space and modality of execution, gesture-speech relation.

Results:

Analyses show significant differences between the 3 groups in many of the investigated domains. The total number of gesture is significantly lower in ASD group both in comparison with TD ($p=,000$) and SD group ($p=,000$). As for gestures function, only ASD children use instrumental gestures; they use significantly less deictic and

ideative gestures in comparison with both the TD ($p=,000$; $p=,003$) and the SD group ($p=,000$; $p=,000$). Further differences emerge from the analysis of gestures' quality: children with ASD tend to produce gestures in a peripheral space, usually not alternating gaze between partner and object. Furthermore, in ASD group a motor asymmetry is present when gestures are executed with both hands, and gestures tend to be more frequently embodied by mothers. Specific correlations between gestural production, cognitive development and autism severity scores have also been investigated.

Conclusions:

Through a detailed analysis of gestures during mother-child interactions, this study identified: specific characteristics of gestural communication in ASD; atypical patterns in motor symmetry which seem to reply what have been found in previous developmental stages (Esposito e Venuti, 2008); correlations between cognitive function, ASD severity scores and gestural performances.

Our results confirm that gestures could be promising candidates for representing an overall synthesis of ASD core difficulties, integrating the socio-communicative realm with that of action and representation. The role of gesture analysis for structuring models of intervention could be an important future area of investigation.

164.151 151 Autistic Features Observed in Young People Who Have Experienced Early Maltreatment – Examining 'Quasi-Autism'. V. Livermore-Hardy^{*1}, D. H. Skuse², M. DeJong¹, L. Brown-Wright¹, M. Murin³ and W. Mandy⁴, (1)Great Ormond Street Hospital, (2)Institute of Child Health, UCL, (3)Great Ormond Street Hospital for Children NHS Foundation Trust, (4)Faculty of Brain Sciences, UCL

Background:

Remarkably little research has considered the long-term impact of abuse and maltreatment in childhood, on the development of social communication. Patterns of autistic-like behaviours appear to be evident amongst children who have been exposed to profound and prolonged institutional deprivation. This has been referred to as 'quasi-autism' in the literature. Within this group, the features that originally

appeared to be consistent with autism were shown to diminish somewhat with age, but a number of atypical features remained. Despite well documented deficits, the parameters for 'quasi-autism' are far from clear-cut. This study aims to further understand the concept of 'quasi-autism' by comparing children who have experienced early maltreatment to children diagnosed with Autism Spectrum Disorder (ASD). In this way the social communication impairments displayed by maltreated children can be more accurately conceptualised.

Objectives:

To investigate whether early maltreatment and abuse influence the development of social communication skills and contribute to the development of features consistent with ASD. If yes, are these features similar to those children who have not experienced such early adversity but do have a diagnosis of autism?

Methods:

12 maltreated children (mean age 11.25 years, mean verbal IQ 82.5) were identified through a national attachment and trauma clinic and assessed for ASD symptomatology (using the 3Di and ADOS) and additional co-morbidities (using the Strengths and Difficulties Questionnaire-SDQ). These children were then matched on verbal IQ and age to a sample of children who had received a clinic consensus diagnosis of high functioning ASD (mean age 11.3 years, mean verbal IQ 84.5). All participants were in mainstream school and had fluent language.

Results:

Using standardised diagnostic measures, no significant differences between the two groups were found. However, a number of non-significant trends were suggested by the data. Although matched on verbal IQ, compared to those with a history of maltreatment (mean=79.7, SD=10.4) the children with ASD (mean=87.9, SD=18.4) demonstrated a trend of higher performance IQ. Parents and carers also reported a trend that children with ASD (mean=2.18, SD=2.18) exhibited greater levels of repetitive, stereotypic behaviours than the maltreatment children

(mean=1.70, SD=1.41). However, using SDQ scores children in the maltreated group (mean=2.90, SD=2.91) were reported to exhibit greater internalising difficulties compared to the ASD group (mean=5.64, SD=3.50). When examining specific 3Di items, children in the maltreated group were significantly more likely to display indiscriminate familiarity ($p < 0.05$), whereas children with ASD exhibited a trend of greater levels of wariness on meeting a stranger.

Conclusions:

In this preliminary study, using fine-grained diagnostic instruments (3Di, ADOS and WISC IV), the two groups in our sample did not show large differences. However our data does not preclude the possibility that these groups show subtle but measurable cognitive and behavioural differences. As we continue to increase our sample size we aim to test our hypotheses that children with 'quasi-autism' difficulties can be distinguished from children with ASD, on the following:

1. Lower repetitive behaviour
2. Less sensory sensitivity
3. Lower non-verbal reasoning skills
4. Greater social disinhibition
5. Greater internalising difficulties

164.152 152 Bullying Involvement and Social Information Processing of Dynamic Social Scenes in Children and Adolescents with ASD. J. H. Schroeder*, J. M. Bebko, M. C. Cappadocia and D. Pepler, *York University*

Background:

Several studies report that individuals with ASD are at an increased risk of bullying victimization in comparison to the general population (e.g. Cappadocia et al., 2011), yet few studies have used Crick and Dodge's (1994) Social Information Processing (SIP) model to explore some of the underlying social processing difficulties in ASD. Two studies have found differences between ASD and children with typical development in the encoding and response generation stages of SIP, but not in the intent attribution stage (Embregts et al., 2006; Meyers et al., 2006).

Objectives:

To develop a better understanding of bullying involvement and the associated encoding, attribution, and response generation stages of SIP in individuals with ASD compared with typically developing (TD) peers.

Methods:

Participants to date are 22 children with ASD (6-16 years; 50% Asperger) and an age- and IQ-matched TD group of 20. Additional data collection is ongoing. Frequency of bullying victimization within the past month was determined using the PREVNet parent report survey. For the Social Information Processing Application (SIP-AP, Innovation Research & Training, 2011), participants watched a series of eight brief videos depicting social situations involving either hostile or ambiguous provocations. The Tobii Eyetracker recorded where participants were looking during the videos. To assess encoding, participants were asked to describe what happened in the video and errors were counted. For intent attribution, participants rated the degree to which the provocateur intended to be mean on a 5-point Likert scale. To assess response generation, participants were asked what they could do if the provocation happened to them.

Results:

Bullying involvement was significantly associated with sample $\chi^2(1) = 8.64, p = .003$. As expected, parents of children with ASD reported more frequent physical, verbal, and social victimization (30 - 45%) than the TD comparison group (5-15%). Consistent with previous studies, the ASD group was significantly more likely than the TD group to make errors during the encoding stage of processing $\chi^2(1) = 4.25, p = .04$. Over two-thirds of children with ASD, relative to only one-third of the TD group, made encoding errors and both groups made more errors during hostile videos. Eyetracking data are currently being analysed. It is hypothesized that the ASD group will spend a smaller proportion of time attending to faces than their TD counterparts. Consistent with previous literature, independent-sample t-tests revealed no significant differences in intent

attributions between the ASD and TD groups (all $ps > .35$). Preliminary analyses of the data reveal a greater mean number of responses generated by the TD group relative to the ASD group. The proportion of assertive responses was greater in the TD group, and the proportion of aggressive responses was greater in the ASD group.

Conclusions:

This is the first study to examine both bullying involvement and social information processing in children with ASD and the first to incorporate an eye-tracking component with an ASD sample. Results will contribute greatly to the understanding of social difficulties in ASD and may help guide treatment planning by targeting specific processing issues.

164.153 153 Challenging Stereotypes: Sexual Functioning of Single Adults with High Functioning Autism Spectrum Disorder. S. Nichols*¹, S. Byers² and S. Voyer², (1)ASPIRE Center for Learning and Development, (2)University of New Brunswick

Background: Healthy and safe sexuality for individuals with autism spectrum disorders (ASDs) is an important developmental goal, yet it has received little empirical attention. What research has been done has focused primarily on negative markers and problematic sexual behavior. In order to be proactive and preventative, studies of the sexual well-being of individuals with ASDs need to address positive sexuality development and barriers to healthy sexuality.

Objectives: The aim of the current online study was to examine the sexual functioning of single adults (61 men, 68 women) with high functioning autism (HFA) and Asperger Syndrome (AS) (had received a score at or above the recommended cutoff (32 out of 50) on the Autism Quotient) living in the community with ($n = 76$) and without ($n = 53$) prior relationship experience (had been in a relationship of at least 3 months).

Methods: Participants completed a set of online questionnaires assessing autism symptoms, psychological functioning, and various aspects of sexual functioning. We examined whether men and women in the two relationship groups differed in their sexual functioning using a 2 (gender) X 2 (group) MANOVA with 10 sexual functioning variables (e.g., Sexual Knowledge, Sexual

Anxiety, Sexual Arousability, Solitary Desire, Dyadic Desire) as dependent measures.

Results: In general participants reported positive sexual functioning. Participants without prior relationship experience were significantly younger and more likely to be male and identify as heterosexual. They reported significantly higher sexual anxiety, lower sexual arousability, lower dyadic desire, and fewer positive sexual cognitions. The men reported better sexual function than did the women in a number of areas.

Conclusions: This study contributes to the literature by providing information about how single men and women with HFA/AS living in the community experience their sexuality across a wide range of positive and negative domains. The results counter negative societal perceptions about the sexuality of high functioning individuals on the autism spectrum, and raise important issues for future study (e.g., understanding sexual preference, promoting women's positive sexuality). These results must be interpreted in light of both the limitations and strengths of the study. As the study comprised an online community sample, we cannot be sure all participants met criteria for a diagnosis of ASD, and the results may have been affected by volunteer bias. However this research represents an important step in characterizing the sexual functioning of men and women with HFA/AS, a step that is particularly noteworthy because there has been so little research to date on sexuality and ASD.

164.154 154 Cognitive-Behavioral Differences in Children with Autism Spectrum Disorder Predicted by Sex-Age. T. A. Knaus¹, J. L. Kamps² and A. L. Foundas*¹, (1)*Louisiana State University Health Sciences Center - N.O.*, (2)*Children's Hospital*

Background: There is a male-predominance in autism spectrum disorder (ASD), supporting the hypothesis that sex-linked factors may be associated with neural risk that could be reflected in performance differences in cognitive-behavioral measures, with age-related divergence. Results of previous studies examining sex differences have been inconsistent and age effects on potential sex differences have not been established.

Objectives: The purpose of this study was to investigate potential sex-linked cognitive-behavioral differences in younger (2-5 years) and older (6-19 years) children with ASD by examining cognitive abilities and autism symptoms in a large clinical cohort (N=505).

Methods: Two groups (Younger, n=300, Older, n=205), evaluated at the Autism Clinic at Children's Hospital between 2005 and 2012, were compared on estimated full-scale IQ (Mullen Scales of Early Learning in Young; Wechsler Scale, Leiter, or Mullen in Older group). The ADOS and parent report measures (Behavior Assessment System for Children; BASC and Adaptive Behavior Assessment System; ABAS) were also examined.

Results: In both age groups, there were more males (Young n=250, Older n=164) than females (Young n=50, Older n=41) with ASD (Male-to-Female Ratio=5:1 Young; 4:1 Older). The younger group tended to be more impaired than the older group. ASD subtypes by age-sex groups were as follows: young girls - 76% autism, 24% PDD-NOS; young boys - 64% autism, 34% PDD-NOS, 2% Asperger; older girls - 44% autism, 41% PDD-NOS, 15% Asperger; older boys - 45% autism, 40% PDD-NOS, 15% Asperger. The young group had fewer verbal individuals (Girls=18%; Boys=29%) than the older group (Girls=78%; Boys=84%). A different profile of sex differences in cognitive abilities was found for young compared to older children. In 2-5 year olds, there were no significant sex differences in visual reception (p=.069) or receptive or expressive language (p=.159), but there was a trend for lower expressive language scores (p=.055) in females compared to males. In older children, there were no sex effects for verbal IQ (p=.249), but a significant sex difference in performance IQ (p=.036), with females having lower scores than males. There were no sex differences in ADOS social or communication scores in either age group. When sensory interests, hand mannerisms, and repetitive behaviors were examined, there was a sex effect (p=.044) in the young group, with girls having higher scores (more impairments) than boys. Parent report measures of communication, social, and motor functioning revealed no sex differences in either age group.

Conclusions: These results suggest some subtle sex differences in cognitive and clinical measures in children with ASD, which vary with age. Specifically, girls in the younger group tended to have more language and motor impairments (slightly more nonverbal individuals, trend for lower expressive language, more sensory interests/hand mannerisms/repetitive behaviors) than boys, whereas in the older group differences emerged in nonverbal abilities, with males outperforming females on performance IQ. Further study is warranted to examine these trends in a longitudinal cohort.

164.155 155 Comparing Grammatical Items in Spontaneous Speech Vs. Parent Report in ASD. A. T. Tovar*, C. A. Navarro-Torres, M. Jyotishi, A. Goodwin, D. A. Fein and L. Naigles, *University of Connecticut*

Background: The Vineland Adaptive Behavior Scales (Sparrow et al., 1984) uses parental report to examine communication and social skills in children with ASDs, and exhibits high reliability when compared with children's actual pragmatic usage (Reichow et al., 2008). However, specific grammatical items (e.g., wh-questions, tense/aspect, negation) may be less reliable, given how widely varying these are in the language development of children with ASDs (Goodwin et al., 2012; Tager-Flusberg, 1994). Moreover, parents may be more sensitive to some grammatical items than others. The current study takes a longitudinal approach, comparing parental report on the Vineland of wh-questions, verb tense, and negation with the children's concurrent spontaneous production. Comparisons are made between high-functioning and 'middle-functioning' groups of children with ASD.

Objectives: We investigate the degree to which parental report of children's grammatical usage on the Vineland 'matches' those children's production in spontaneous speech.

Methods: Eleven ASD children ($MA=31.23$ months) were assessed every four months for two years. HFA ($n = 5$) children had Mullen scores in the normal range at visit 1; MFA ($n = 6$) children produced the target grammatical items but had Mullen scores at least 1.5 SD below the normal range at visit 1. At each visit, the children participated in a 30-minute semi-structured play session with their parent. All speech was transcribed and coded for types and tokens of Wh-

questions, progressive and regular past verb inflections, and negation. At each visit, the Vineland was also administered, and coded for parental report of the child producing *what/where, who/why, and when* questions, verbs ending in "-ing" and "-ed", and negatives in sentences. Data were analyzed into three categories: Vineland and Speech at same levels, Vineland more advanced than Speech, and Vineland less advanced than Speech.

Results: Chi-squares were performed across visits for each group separately, and combining visits to compare groups. For negation, 88-90% of Vineland-Speech comparisons were at the same level, and this did not differ across visits nor across subgroups. In contrast, for wh-questions, only 46% of Vineland-Speech comparisons were at the same level; 34% showed Vineland more advanced than Speech and 20% showed Speech more advanced than Vineland. Moreover, this distribution varied significantly by subgroup ($X^2(2) = 14.13, p < .001$), with more Speech-more-advanced-than-Vineland children in the MFA group. For both verb inflections, 71% of Vineland-Speech comparisons were at the same level, 11% showed Vineland more advanced than Speech, and 18% showed Speech more advanced than Vineland. This distribution varied significantly by subgroup for the progressive inflection, ($X^2(2) = 10.5, p < .05$), but not for the regular past. Again, more children in the MFA group produced progressive inflections in Speech than were reported to do so by their parents.

Conclusions: Parental report in the Vineland varies in how consistently it captures children with ASDs' production of grammatical items. Production of negation use was highly accurate; however, production of progressive inflections, and especially wh-questions, was under-rated, particularly with children in the middle range of language use.

164.156 156 Defining the Intellectual Profile of Elderly Persons with an Autism Spectrum Disorder. L. Ham¹, A. A. Spek², R. Wilting³ and F. Geven³, (1)GGZ Eindhoven Adult Autism Center, (2)Mental Health Institution Eindhoven, (3)GGZ Eindhoven Center Elderly Care Autism

Background:

Very little is known about autism spectrum disorders (ASD) in the elderly. Although research

showed that behavioral symptoms of ASD seem to become somewhat less intrusive over time, it is not clear whether this is related to cognitive improvement. It is also unclear if the aging process in adults with ASD is similar to that of the general population. Research into older persons with ASD is limited to a few case reports and one study in which executive functions and memory were examined. It is expected that the population of elderly individuals with ASD will grow substantially in the coming years, because autistic spectrum disorders are increasingly being recognized in adults and in elderly individuals. Therefore, it is important to gain knowledge about ASD in older people, their strengths and weaknesses and their specific needs.

Objectives:

To examine the WAIS III profile in older persons with ASD.

Methods:

23 elderly male individuals (age 60+) with ASD were compared with 23 neurotypical older male adults. Both groups were matched on age and level of education. Intelligence profiles were examined using the WAIS-III. Diagnoses of the ASD-group were based on the current algorithm of the ADI-R and an interview based on DSM-IV criteria of ASD.

Results:

Results showed no differences in total intelligence between the two groups. The ASD group performed significantly weaker on the index scale Processing speed. The other three index scales did not differ between the two groups. On subtest level, impairment was found in the ASD group on symbol search, no differences were found on the other subtests.

Conclusions:

It was concluded that the intelligence profiles of elderly with and without ASD are in many ways similar, except for processing speed, in which the elderly with ASD are relatively impaired.

164.157 157 Developmental Aspects of Affective Decision Making in ASD. D. Bjornn*¹, S. Wigham², L. Gray³, P. D. Chamberlain¹, K. Ames¹, S. White⁴, T. Newton¹, M. South¹ and J. Rodgers⁵, (1)Brigham Young University, (2)Newcastle University Institute of Health and Society, (3)Newcastle University, (4)University of California, Davis, (5)School of Medical Sciences, Newcastle University

Background: We previously presented data showing superior behavioral performance in ASD on an affective decision making task (the Iowa Gambling Task; IGT), in a sample of young, high-functioning ASD adolescents (ages 11-16) compared to age- and IQ-matched typical controls. Because there was no correlation in the ASD group between behavioral performance and anticipatory skin conductance response, we suggested that the ASD group used a hyper-rational strategy to achieve good results. However, we also noted significant correlations with age in both ASD and the typical (TYP) group and wondered how different developmental trajectories may influence the interaction of rational versus emotional strategies for completing the IGT. We have since collected IGT data for 50 additional children ages 8-11 to investigate age-related influences.

Objectives: To explore how participant age influences both strategy and performance during decision making on the IGT and how this influence may differ across ASD and typical development.

Methods: The Iowa Gambling Task presents two decks of cards that have big gains but also occasionally large losses, resulting in overall net loss; and two decks with smaller gains but also relatively smaller losses, resulting in overall net gain. We report behavioral data for 136 participants ages 8-16 (69 ASD, 67 TYP; mean age=12.6, Full Scale IQ mean=110). Skin conductance response data were available for a subsample of 88 (42 ASD) participants. We analyzed younger versus older age groups split at the cut of 12.5 years that was reported by Schumann et al. (2004) for changes in the trajectory of amygdala growth in ASD.

Results: Behavioral data of the number of "good" versus "bad" deck choices across 5 blocks of 20 trials, using a larger sample that also includes a younger age range, again shows significantly overall better performance in the ASD than TYP

group. Older children outperform younger children across both groups, however the relative superiority of ASD performance persists even at younger ages, including a significant 3-way interaction of diagnosis x age x trial block of choices. Analysis of anticipatory SCR before making choices from bad decks versus good decks shows that the younger ASD group, but not the older ASD group, shows greater SCR response before choosing bad than good decks; there is no such differentiation at all in the TYP group.

Conclusions: These data may represent a functional example of Schumann et al.'s (2004) hypothesis of overactive amygdala function in younger children with ASD that slows in later adolescence. The ASD group is more successful than controls in both groups but may depend on different strategies (gist-based versus rational-based) across development. The failure of the TYP group to perform well at any age, using the task software published by the task authors, is surprising although recent work (see Smith, Xiao & Bechara, 2011) shows that typical adolescents at least have difficulty inhibiting impulsive reward-based choices. The mechanisms of decision making in ASD vis-à-vis typical development remain poorly understood and more research here is needed, in addition to work on the effects of age.

164.158 158 Feasibility of Experience Sampling Methodology in Understanding Everyday Experience in Autism Spectrum Disorders: A Pilot Study. Y. W. Chen*¹, A. C. Bundy¹, R. Cordier² and S. L. Einfeld¹, (1)University of Sydney, (2)James Cook University

Background: Many researchers have identified high levels of loneliness in individuals with autism spectrum disorders (ASD), interpreting these findings as a desire to engage socially. However, exploring how daily contexts influence everyday social participation from their perspectives is needed to better understand their loneliness and desire for social inclusion. Furthermore, even though some researchers have interviewed people with ASD, the rich data generated through in-the-moment reporting has great potential as an alternative method, rather than relying on retrospective data gathered in interviews. Experience sampling methodology (ESM), an idiographic tool, has been widely used in typical and clinical populations to capture individuals' behaviours, thoughts, and emotions in real time

and in natural contexts. ESM can assist to develop individualised approaches for addressing loneliness and promoting social engagement. However, to date, very few studies have used ESM to examine the relationships between daily contexts, thoughts and feelings as internal experience of people with ASD.

Objectives: The pilot study aims to identify the feasibility of using ESM to explore everyday experience in individuals with ASD in preparation for a larger study.

Methods: Two people with Asperger's syndrome, a male aged 23 and a female aged 31 years, were asked to carry an iPod Touch which prompted them randomly, 7 times/day for 7 days, to repeatedly respond to a short questionnaire (less than 2 minutes in duration) regarding what they were doing, why, with whom, how they felt and what they thought about the involved situation. Semi-structured interviews were completed at the end of sampling. The reasons for activity engagement were then coded into intrinsic motivation, extrinsic motivation and amotivation for analysis. Reliability of the method was examined by comparing means of each participant's internal experiences between the first and second halves of the week, while validity was investigated by calculating z-scores to account for variation in individual reporting.

Results: The participants responded to the questionnaire 45 and 31 out of 49 times, respectively. There were no significant differences in internal experience, except being involved, between the first and second halves of the week. Compared with responses with extrinsic motivation and amotivation, the responses with intrinsic motivation showed high levels of enjoyment and interest in activity, and preferring to continue the same activity. These findings support the internal validity of the method. In addition, moderate correlations between internal experience (i.e., interest in activities, being involved, enjoyment and anxiety) as well as between loneliness and aspects of reciprocal interaction (i.e., being listened to and caring for others) illustrated the questionnaire can sensitively capture internal experience and thoughts. The participants reported that the questions were straightforward and the method

was easy and convenient, although the prompting slightly interfered with their daily activities.

Conclusions: The study has illustrated the feasibility of using ESM in people with ASD to self-report their engagement in daily life by reflecting on their own mental states and thoughts. The study supported the use of ESM for examining internal experience and the impacts of social contexts on everyday experiences in individuals with ASD.

164.159 159 Food Selectivity, Weight Status, and Caregiver Feeding Practices in Children with Autism Spectrum Disorders. T. V. Kral*¹, M. C. Souders², W. T. Eriksen¹, A. M. Remiker³, V. H. Tompkins¹ and J. A. Pinto-Martin¹, (1)*University of Pennsylvania School of Nursing*, (2)*University of Pennsylvania School of Nursing/The Children's Hospital of Philadelphia*, (3)*University of Pennsylvania Perelman School of Medicine*

Background: To date limited research exists which has examined eating behaviors and diet quality among children with developmental abilities, including children with autism spectrum disorders (ASD). A small number of studies suggest that children with ASD are picky eaters and show aversions to certain textures, smells, colors, temperatures, and brand names of foods, all of which can adversely affect their dietary intake. Further, very little is currently known about feeding practices that caregivers of children with ASD may develop to address problematic eating and nutritional difficulties in their children.

Objectives: The aim of this cross-sectional study is to examine weight status/adiposity, eating behaviors including food neophobia (children's reluctance to eat and/or avoid novel foods) and caregiver feeding practices in an urban sample of 4- to 6-year-old children with ASD and typically developing children (TDC).

Methods: Caregivers of children with ASD (n = 12) and TDC (n = 20) were asked to complete a series of validated questionnaires, including the Child Eating Behavior Questionnaire, Child Food Neophobia Scale, Child Feeding Questionnaire, and Parental Feeding Style Questionnaire, to assess their children's eating behaviors as well as their own feeding practices. During an onsite visit to the Center for Autism Research at the Children's Hospital of Philadelphia and the Center

for Weight and Eating Disorders at the University of Pennsylvania children's height, weight, waist circumference, and skinfold thickness were measured. The study is ongoing and data presented here will be augmented by additional data.

Results: Preliminary findings indicate that 50% of children with ASD and 25% of TDC were considered overweight or obese (BMI-for-age \geq 85th percentile; $P = 0.15$). Further, children with ASD, when compared to TDC, had a greater waist circumference (57.9 ± 8.9 vs. 52.0 ± 4.3 cm; $P = 0.02$) and BMI z-score (1.1 ± 1.4 vs. 0.2 ± 1.1 , $P = 0.06$). In terms of eating behaviors, children with ASD were reported to be significantly more selective about the range of foods they accepted (4.0 ± 0.2 vs. 2.5 ± 0.1 ; $P < 0.001$) and showed overall greater food neophobia (3.5 ± 0.2 vs. 2.6 ± 0.2 ; $P = 0.002$) and less enjoyment of food (3.2 ± 0.2 vs. 3.8 ± 0.2 ; $P = 0.057$) than TDC. Caregivers of children with ASD reported engaging in significantly more prompting and encouraging their children to eat (3.9 ± 0.2 vs. 3.2 ± 0.2 ; $P = 0.03$), instrumental feeding (2.1 ± 0.1 vs. 1.6 ± 0.4 ; $P = 0.03$), and emotional feeding (1.9 ± 0.2 vs. 1.3 ± 0.1 ; $P = 0.03$) than caregivers of TDC.

Conclusions: These preliminary results suggest that despite being more selective in their food choices and showing enhanced food neophobia, children with ASD appear to be at an increased risk of excess weight gain. This, in turn, puts them at greater risk of chronic diseases associated with obesity. Future studies are needed that evaluate the effectiveness of strategies that caregivers use to counter nutritional difficulties and promote healthy eating in their children.

164.160 160 Intelligence Profiles in Children and Adolescents with 22q11 Deletion Syndrome with and without Psychopathology. E. Hidding*¹, H. Swaab², J. A. Vorstman³, H. van Engeland⁴ and L. M. J. de Sonneville¹, (1)*Leiden University*, (2)*Leiden University, Faculty of Social Sciences*, (3)*Brain Centre Rudolf Magnus*, (4)*Rudolf Magnus Institute of Neuroscience, University Medical Center Utrecht*

Background: In patients with 22q11 deletion syndrome (22q11DS) neural developmental patterns are found that seem to be related to a greater vulnerability for the development of psychopathology. High incidence of Autism Spectrum Disorders (ASD) is frequently reported

and 25-30% of patients develop psychotic disorders in particular schizophrenia. Some studies report that girls often outperform boys, and younger children show higher intelligence scores than older patients. These findings suggest that gender and age may affect cognitive variability in patients. Studies so far are inconclusive in this regard and focused mainly on intelligence profiles on full-scale level or differences between verbal and performance intelligence. Possibly, these cognitive differences are associated with variable vulnerability for psychiatric disorders in these patients.

Objectives: To perform an in depth analysis of intelligence profiles in children and adolescents with 22q11DS and investigate the influence of gender, age and psychopathology.

Methods: Intelligence assessment of sixty children and adolescents aged 9 to 18.5 years using age appropriate Wechsler scales of intelligence as well as psychological assessment, using standardized interview methods to evaluate psychopathology.

Results: Significant higher intelligence scores were found on Full Scale IQ, Verbal Comprehension and Processing Speed for female patients as compared to male patients. On a subtest level these differences were also found on three out of twelve subtests. Children showed also higher FSIQ and Processing Speed scores as compared to adolescents and performed also better on three of the twelve subtests. When comparing patients with and without psychopathology a significant interaction between presence of Autism Spectrum Disorders and age was found. In patients with ASD relative comparable FSIQs were found in children as well as in adolescents, whereas in patients without ASD a higher FSIQ was found in children while a lower FSIQ was found in adolescents.

Conclusions: Findings highlight the heterogeneity of the 22q11DS population as well as the importance of investigating intelligence on multiple levels. Processing Speed appeared to be more impaired in boys as compared to girls and older patients also had more difficulties with tasks requiring this skill. The age-associated differences found between patients with and without ASD suggest different developmental cognitive

trajectories for these subgroups of patients. These findings provide new perspectives on investigating the relation between cognitive functioning and psychopathology in a developmental context in patients with 22q11DS.

164.161 161 Is There an Optimal Developmental Path in Autism?.
M. Dawson¹ and I. Soulières*², (1)*Centre d'excellence en Troubles envahissants du développement de l'Université de Montréal (CETEDUM)*, (2)*University of Quebec in Montreal*

Background: Two striking features of autism are diversity in reported developmental paths and diversity in reported autistic outcomes, from outstanding to extremely poor. Current approaches to autism posit the existence of an optimal developmental path, against which the potential of autistics can be judged and thus their outcomes predicted. However, long-term follow-up studies of diagnosed autistics present a more complex picture (e.g., Howlin, 2011), while existing epidemiology suggests that many older autistics are undiagnosed (e.g., Brugha et al., 2011; Kim et al., 2011). Further, the apparent consensus that early development, particularly speech onset timing, cannot be used for diagnostic subgrouping (APA, 2012) calls into question its ostensibly crucial role in determining autistic outcomes.

Objectives: We aimed to verify whether speech onset timing is related to later (school-aged and older) outcomes of concern in autistic spectrum individuals subgrouped according to presence or absence of speech development anomalies. We also aimed to compare later outcomes as assessed via three different instruments, in autistic children and autistic adults subgrouped in the same way. This study builds on data we presented at IMFAR 2007.

Methods: We retrieved three data sets from consecutive cases from the Riviere-des-Prairies Hospital database who were six years of age or older and had an autism (with speech development anomalies) or Asperger syndrome (without speech development anomalies; normal-range Wechsler IQ) best estimate clinical diagnosis and ADI-R evaluation above threshold for autism. First and second sets included all individuals with valid age of first words and phrases ADI-R data, as well as Wechsler IQ (first set) or Vineland scores (second set). The third set included all individuals with Wechsler IQ, Raven's

Progressive Matrices, and Vineland adaptive behavior scores.

Results: For autistics (N=90) there was no significant correlation between age at first words or phrases and Wechsler full-scale, verbal, and performance IQ, or (N=61) Vineland scores. There was no significant difference between autistics with 70 or above versus below 70 FSIQ, in age of first words (mean respectively 29.3 versus 32.8 months, $p=.46$) or phrases (41.7 versus 43.6 months, $p=.64$). For Asperger individuals (N=39), there was no significant correlation between age of first words and FSIQ, VIQ or PIQ, or between age of first phrases and VIQ. However, there was a significant correlation between age of first phrases and both FSIQ and PIQ. As with autistics, for Vineland scores (N=29) there was no correlation with either age at first words or phrases. Comparisons of Wechsler, Vineland, and Raven scores in autistic and Asperger participants revealed dramatic discrepancies across measures in both adults and children, and higher Wechsler and Raven scores in autistic adults versus children.

Conclusions: Speech onset timing is unrelated to later IQ or adaptive behavior scores in autistic individuals defined by speech development anomalies. Different instruments can give dramatically different portraits of autism spectrum outcomes. Data from short-term studies and/or biased samples (e.g., samples excluding later-diagnosed autistics) may be distorting current conceptions of outcome predictors and limiting our knowledge of how atypical developmental paths lead to outcomes in autism.

164.162 162 Longitudinal Changes in Processing Speed and Corresponding White Matter Microstructure in Autism Spectrum Disorder (ASD). B. G. Travers^{*1}, E. D. Bigler², N. Adluru¹, D. P. Tromp¹, C. Ennis¹, M. Prigge³, A. L. Froehlich³, N. Lange⁴, A. L. Alexander¹ and J. E. Lainhart⁵, (1)University of Wisconsin, (2)Brigham Young University, (3)University of Utah, (4)McLean Hospital, (5)Waisman Center, University of Wisconsin-Madison

Background: Slower processing speeds have been commonly reported in individuals with ASD (Mayes & Calhoun, 2003, 2008; Oliveras-Renta et al., 2011; Wechsler, 2003). However, little is known regarding how processing speed matures and develops from childhood into adulthood in this population. Given that processing speed is a

fundamental cognitive process that relates to higher order skills such as communication ability, it is important to examine processing speed changes over time in ASD. Further, it is important to examine underlying neural substrates of processing speed that may be affected in ASD.

Objectives: To compare longitudinal measures of processing speed from early childhood to adulthood in persons with ASD and typically developing controls, and to examine whether processing speed depends on the average fractional anisotropy (FA) of whole-brain white matter, as measured with Diffusion Tensor Imaging (DTI).

Methods: In our accelerated longitudinal design, participants included 86 males with ASD (age range 6.3-42.6 years) and 60 males with typical development (age range 6.9-39.8 years). Participants completed standardized processing speed measures of the Wechsler Intelligence Scale for Children, 3rd edition (WISC-III) and the Wechsler Adult Intelligence Scale, 3rd edition (WAIS-III) 1-3 times over the last 10 years. Linear mixed effect models examined processing speed measures as a function of diagnostic group and age, while controlling for full-scale IQ. Pearson correlations (r) were used to quantify the relation between processing speed index scores and average whole-brain FA.

Results: After accounting for age, full-scale IQ, and individual growth curves, persons with ASD scored on average 12.0 points lower than typically developing controls on the processing speed index (PSI) of the WISC-III and WAIS-III ($p < .001$). Group differences also emerged in the raw scores of the WAIS-III coding ($p < .001$) and symbol search subtests ($p < .001$), but not in the raw scores of the WISC-III coding ($p = .10$) or symbol search subtests ($p = .19$). There were no significant age-by-group interactions. Collapsing across all time points, whole-brain average FA was correlated with PSI scores when both groups were included in the model, $r(149) = +.23$, $p = .005$, but not within each group separately, ASD: $r(93) = +.12$, $p = .25$; TD: $r(55) = +.19$, $p = .15$. This small-sized correlation further diminished across all participants when age was included as a covariate.

Conclusions: Individuals with ASD exhibited slower processing speed index scores across a wide age range (6-42 years) compared to individuals with typical development. However, group differences in subtest raw scores were only significant in the adult versions of the test. These results suggest that processing speed impairments are present in ASD and may be more pronounced in adult IQ tests, even though the rate of age-related processing speed changes were similar across groups. The average FA of the whole-brain white matter was not related to processing speed index scores when age was included in the model. Future analyses will examine correlations between processing speed and region-specific white matter tracts, as well as correlations between processing speed and ASD symptom severity measures.

164.163 163 Mapping Development Change in Hypersensitivity to Pitch in Children, Adolescents, and Adults with ASD. P. Heaton*¹ and J. Mayer², (1)*Goldsmiths College, University of London*, (2)*University of Roehampton*

Background: Whilst enhanced pitch perception has been reported in a large number of studies of individuals with ASD (Bonnell et al., 2003, 2010; Heaton, 2003, 2005; Heaton, Hermelin, & Pring, 1998, 1999; Heaton, Hudry, Ludlow, & Hill, 2008; Heaton, Williams, Cummins, & Happé, 2008; Jones et al., 2009; Mottron, Peretz, & Menard, 2000; O’Riordan & Passetti, 2006) little is known about its behavioural consequences and the extent that it may change over time. Previous research carried out with children with ASD has revealed enhanced sensitivity to the psychoacoustic properties of speech but the extent that this is characteristic in adults has yet to be investigated. **Objectives:** The present study aimed to replicate earlier findings of superior pitch discrimination across speech and non-speech stimuli in children with ASD within groups of high-functioning adolescents and adults with ASD. A second aim of the study was to examine the cognitive, clinical, and behavioural correlates associated with enhanced pitch perception in the adult group. **Methods:** The trajectory analysis was carried out on groups of children, adolescents and adults with high-functioning ASD and age and intelligence matched typically developing controls. For the second analysis, cognitive assessments as well as self-report questionnaires were used to assess IQ, communication difficulties, and sensory processing abnormalities associated with superior

pitch discrimination in high functioning adults with ASD and controls. **Results:** The findings showed that whilst levels of discrimination performance did not differ across the child, adolescent and adult groups with ASD, significant increases were observed across all time points in typically developing comparison groups. Correlations carried out on the discrimination data and background data for the adults revealed associations between task performance and working memory scores and autistic symptomatology for the ASD but not the control group. **Conclusions:** The results suggest that the developmental trajectory of pitch discrimination differs in typical development and ASD and that unique associations between pitch discrimination and core features of autism and working memory are characteristic in high-functioning adults with ASD.

164.164 164 Perspective Taking Abilities in Aging Adults with ASD: An Exploratory Study. A. G. Lever* and H. M. Geurts, *University of Amsterdam*

Background: Understanding a faux-pas requires complex perspective taking abilities, like attributing mental states to oneself and others and use them for explaining and predicting behavior. More precisely, it involves the ability to recognize two mental states: one of the speaker who unintentionally says something socially inappropriate and one of the listener on whom the statement has an impact. Previous research in autism spectrum disorders (ASD) and in neurotypical aging on perspective taking is inconsistent and the effect of age has never been investigated among adults with ASD. Therefore, this study focuses on perspective taking in adults with ASD.

Objectives: To explore 1) how adults with ASD perform on a faux-pas perspective taking test and how they report themselves on their perspective taking abilities; 2) whether and how these two measures relate to each other; and 3) the effect of age on perspective taking in adults with ASD.

Methods: We compared perspective taking performance on a faux-pas test (Stone, Baron-Cohen, & Knight, 1998) to self-reported perspective taking abilities on the Interpersonal Reactivity Index questionnaire (IRI; Davis, 1980, 1983) of 29 adults with ASD and 23 neurotypical adults between 19 and 74 years old. Dependent

measures were scores on the IRI perspective taking subscale and faux-pas scores on the faux-pas and control stories composing the faux-pas test.

Results: Individuals with ASD presented impaired performance on the faux-pas stories. More detailed analysis revealed that adults with ASD did not differ on the detection of the faux-pas or the associated false belief, but on the explanation given to the faux-pas. Individuals with ASD were also impaired on control stories. They more often misinterpret a socially normal situation, considering it as socially awkward. Groups also differed on self-reported perspective taking: adults with ASD reported lower perspective taking abilities than neurotypical adults. Self-report was positively correlated with performance on the faux-pas ($r=.33$) and control ($r=.46$) stories. Exploratory analyses revealed that age did not influence any of the dependent measures.

Conclusions: We provide evidence that, although adults with ASD recognized a discrepancy between the speaker's perspective and the listener's perspective, they were not able to explain the reason of the socially inappropriate response. Moreover, adults with ASD presented more difficulty in interpreting straightforward situations. However, they showed to have insight into their own perspective taking difficulties, as self-report was associated with test performance. Age does not seem to influence these capacities. These results show the importance of assessing perspective taking abilities not only in awkward, but also in normal, situations. Our results are preliminary and present data from an ongoing research project. We expect to include 40 participants per group in May 2013.

164.165 Predictive Value of Social Communicative Abilities in Toddlers Screening Positive for ASD towards Outcome At Age 7-8y. J. Vermeirsch*, M. Dereu and H. Roeyers, *Ghent University*

Background: Early detection of autism spectrum disorder (ASD) is important for clinical (e.g., to facilitate early intervention) as well as theoretical (e.g., to improve our knowledge about the developmental pathway of the disorder) reasons. Therefore, routine screening for ASD of all children has been recommended (American Academy of Pediatrics, 2007). In recent years,

many screening instruments for ASD in toddlers were developed but they often generate a high false positive rate (e.g., Kleinman et al., 2008). These false positive screen children may have other developmental difficulties that also need thorough assessment and early intervention (e.g., Dietz et al., 2006). However, only a few studies prospectively followed the development of positive screen children into childhood (e.g., Charman et al., 2005) and these studies usually did not include false positive screens.

Objectives: The first aim of this study was to determine if language, intelligence, and theory of mind (ToM) differ in children with and without a clinical diagnosis of ASD at the age of 7-8y, recruited from a group of children with a positive screen for ASD in toddlerhood. Secondly, this prospective study wanted to examine if social communicative abilities in toddlers screening positive for ASD are predictive for outcome at age 7-8y.

Methods: Seventy-nine children were identified as at-risk for ASD based on a positive screen for ASD and were seen at the university lab between ages 2-4 (Dereu et al., 2012). At the age of 3, the early social-communicative skills imitation, joint attention, and pretend play were assessed. At age 7-8y, all children of the at-risk group were asked to participate in a follow-up study to measure their language, intelligence, and ToM. Preliminary results based on one third of the sample are summarized here. At the meeting, complete data will be presented.

Results: Significant differences were found between children who developed ASD and the group who did not for all variables measured at the age of 7-8y. Children with ASD had poorer language skills, a lower IQ, and scored worse on ToM tasks than children without ASD. Hierarchical linear regression analyses revealed that social communicative abilities at age 3y explained unique variance in outcome measures at age 7-8y on top of the variance explained by diagnostic status (total variances explained were between 61% and 91%). Procedural imitation and initiated behavioural requests explained respectively 13-15% and 33-53% additional variance in language, intelligence, and ToM at 7-8y. In addition, initiated joint attention explained respectively 41% and 36% additional variance in language and

intelligence. Finally, pretend play only predicted ToM at age 7-8y (16% additional variance explained).

Conclusions: Social communicative skills measured at 3y can predict outcome at age 7-8y. Especially initiated joint attention and behavioural requests explained additional variance in language, intelligence, and ToM on top of variance explained by diagnosis (true versus false positives). So, thorough assessment of social communicative abilities may also be important in false positive screens and, if impaired, they should be targets of early intervention in at-risk groups.

164.166 166 Reading and Oral Language Comprehension in Students with ASD. N. McIntyre^{*1}, P. C. Mundy², M. Solomon³, N. V. Hatt², M. Gwaltney⁴, W. Jarrold⁵ and K. Kim⁶, (1)*U.C. Davis*, (2)*University of California at Davis*, (3)*Department of Psychiatry, MIND Institute, Imaging Research Center*, (4)*University of California Davis, Learning & Mind Sciences*, (5)*UC Davis*, (6)*MIND Institute, UC Davis*

Background:

A small, but expanding, body of research has indicated that reading comprehension can be challenging for students with ASD. The Simple Model of Reading (Perfetti, Landi & Oakhill, 2005) posits that reading ability is comprised of two processes: (1) word reading ability and (2) oral language processing that creates meaning from the words. This is important because one of the cardinal diagnostic criteria in the DSM-IV for autism is delayed or abnormal functioning in communication and language (APA, 2000). Therefore, it may be that reading comprehension deficits are part of the expression of the social communication symptom domain of the phenotype of ASD.

Objectives:

This study was designed to investigate the role of oral language comprehension in explaining impairments in reading comprehension in a sample of children with high functioning autism (HFA; FSIQ > 80).

Methods:

The study included 29 children with HFA and 36 typically developing control children, who were matched for age (range 8 to 16 years old) and IQ. Diagnosis was confirmed via multiple methods, including the ASSQ (1999), SCQ (1999) and SRS (2003) parent report questionnaires. IQ was measured with the Wechsler Abbreviated Scales of Intelligence (1999), while reading comprehension and oral language comprehension were assessed with the Wechsler Individualized Achievement Test-III (2009).

Results:

Regression analyses revealed significant effects for Diagnostic Group on reading comprehension (RC), $R = .24$, $p < .05$, and oral language comprehension (OLC), $R = .31$, $p < .01$. Follow-up analyses indicated diagnostic group differences were more apparent on these variables for older subgroups of students (12 to 16 years) than for younger subgroups of students (8 to 11 years): for RC, $p < .065$ and OLC, $p < .02$. A multiple regression analysis of RC indicated an effect for Diagnostic Group, $R^2 = .05$, $F(1, 62) = 3.20$, $p < .02$, and effect for OLC, change in $R^2 = .23$, $F(1, 62) = 19.1$, $p < .001$, and the DX by OLC diagnostic term, change in $R^2 = .07$, $F(1, 62) = 6.21$, $p < .02$. The interaction reflected the observation that the correlation between RC and OLC was $.73$, $p < .001$ in the HFA sample but $.30$, $p < .35$ in the TD sample.

Conclusions:

This study provides evidence that students with HFA display impairments both in reading comprehension and oral language comprehension. These impairments were more pronounced in older than younger children. Moreover, a primary observation was that OLC and RC displayed a significantly stronger association in the HFA sample than the TD sample. This supports prior research findings that oral language abilities in children with ASD significantly relate to their reading ability (Jones et al., 2009; Norbury & Nation, 2011; Randi, Newman & Grigorenko, 2010; Ricketts, 2011). Moreover, they raise the possibility that reading comprehension deficits are part of the language communication impairments that are central to the nature of ASD.

164.167 167 Restricted and Repetitive Behaviours in Autism and Typical Development: Group Differences and Associations with Development Over Time. C. Harrop*¹, H. McConachie², R. Emsley¹, K. Leadbitter¹, J. Green¹ and P. Consortium¹, (1)University of Manchester, (2)Newcastle University

Background: Repetitive and restricted behaviours (RRBs) are a key diagnostic feature of autism spectrum disorders (ASD). However these are under-researched compared to other core deficits. As a result little is known about the relationship between RRBs and development or how these relationships change over time. Research has produced mixed findings regarding the relationship between RRBs and non-verbal development (Bishop et al, 2006), language (Militerni et al, 2002) and other aspects of the ASD triad (Bodfish et al, 2000; Caracani-Rathwell et al, 2006). Fluctuation in RRBs in children with and without autism has been shown and is also accompanied by a change in presentation (Turner, 1999); however most research relies upon questionnaire and interview data not direct observation.

Objectives: We used a systematic observation methodology to investigate the presence of RRBs in preschool children with and without ASD at three timepoints during 13 months of development. We predicted that at all timepoints children with ASD would demonstrate elevated levels of RRBs. Continued elevated rates of RRBs were expected in the ASD group, but reduction over time in TD. We hypothesised that a higher incidence of RRBs would correlate negatively with non-verbal development and language, but positively with ASD severity.

Methods: 49 children (mean age at T1 = 44.5 months, SD = 8.53) with ASD were matched to 45 TD children using non-verbal development scores. Children also completed measures of language and play. ASD children completed the ADOS and their parents the ADI-R. Observational coding of RRBs was based on items used in the Repetitive Behaviour Questionnaire (Turner, 1999), DISCO (Wing et al, 2002) and by Watt et al (2008). All RRBs observed within a 10 minute free play session were coded using Noldus Observer.

Results: Significantly more RRBs were observed in the ASD group than the TD group at all timepoints. Children with ASD showed a slight

increase in the number of RRBs over time; however change scores were non-significant. TD children demonstrated a slight increase in RRBs at T2 followed by a decrease at T3. The change between T2 and T3 approached significance ($t = 11.96$; $p = .057$). Despite group differences in RRBs, there was no difference in the rate of change in expression of RRBs. At all three time points, total RRBs correlated negatively with non-verbal development and language irrespective of group. No association was found with ASD severity.

Conclusions: This study supports the view that whilst RRBs are evident in TD, these are less than in preschool children with ASD. In ASD the frequency of behaviours remained constant and did not reduce. Change rates between the two groups, despite the difference in T1 scores, were similar with both groups changing at the same rate. In keeping with the findings of Bishop et al (2006) and Militerni et al (2002), non-verbal development and language associated negatively with heightened RRBs totals. These associations were present in TD children. The lack of association with ADOS algorithm scores is suggestive that RRBs are dissociable from social and communication deficits in ASD.

164.168 168 Savant Skills in a Large Autistic Sample: Prevalence and Relation with Age and Intelligence. P. Jelenic* and L. Mottron, *Centre d'excellence en Troubles envahissants du développement de l'Université de Montréal (CETEDUM)*

Background: Postal surveys, parent report, and/or inspection of Weschler subtest scores within limited sample sizes variously indicate a 10-30% prevalence of savant skills in the autistic population (e.g., Treffert, 2010; Howlin et al., 2009). Contrary to earlier views, savant skills are not solely found in intellectually disabled individuals but may primarily be found in autistics whose measured intelligence, at least on certain instruments or subtests, is within the normal range. Using the ADI-R to investigate savant skills may be a time- and cost-effective method allowing characterizing of savant skills in large samples of autistic individuals.

Objectives: We aimed to investigate in a large autistic population (1) the nature and prevalence of reported savant skills, using scores on ADI-R questions 106-111, and (2) the relation of savant

skills with age, Wechsler FSIQ and Raven's Progressive Matrices (RPM) intelligence scores.

Methods: Our sample included 238 (26 female) autistic participants enrolled in our database and diagnosed with the ADI-R performed by trained clinicians. Participant age range was 2-39 years (mean 11.4) at the time of ADI-R administration. Savant skills are indicated by a score superior or equal to 3 on at least one of Questions 106-111 of the ADI-R on either "current" or "ever" shown behavior.

Results: 61.3% (146/238) of our sample were reported to have savant skills: 28% of autistics age 2 to 5 years, 70% of autistics age 6 to 13 years, and 76% of autistics age 14 years and up. Reported savant skills were significantly more frequent in older participants than in pre-schoolers ($X^2(2) = 32.64, p < .0005$). Among 119 participants for whom both Wechsler and RPM scores were available, those with reported savant skills (93/119) had significantly higher RPM percentile scores (68.9 vs 45.2; $t(117) = 3.423, p < .001$) and significantly higher Wechsler FSIQ (91.8 vs 80; $t(117) = 3.051, p < .003$) than those without reported savant skills.

Among 19 participants with Wechsler FSIQ under 70 (range 40-69), 63% were reported to have savant skills, as were 81% among 100 participants with FSIQ of 70 or higher. The ratio of participants reported as with versus without savant skills was comparable in low versus normal-range FSIQ subgroups, Fisher $p = .126$. Among 10 participants with RPM percentile ranks between 1 and 10, 50% were reported to have savant skills, in contrast to 81% among 109 participants with RPM percentile ranks between 11 and 99. The ratio of participants with versus without savant skills was significantly lower in low versus high RPM percentile rank subgroups, Fisher $p = .039$.

There was an average of 2.3 exceptional abilities reported among the 146 autistic savant participants scoring 3 or 4 on the ADI-R. The most common skills were memory (35%), visuo-spatial (20.5%), followed by reading (13.9%), musical (10.7%), arithmetic (10.1%) and drawing (9.8%).

Conclusions: These results indicate that savant skills are an intrinsic part of autism. Savant skills

are more frequent than previously thought in the autistic population and are mostly evident among older individuals with higher measured intelligence. RPM scores predict savant skills in autism to a greater extent than Wechsler scores.

164.169 169 Self-Perception of Competencies in Adolescents with Attention-Deficit Hyperactivity Disorder and Autism Spectrum Disorders. R. Furlano*, E. A. Kelley, E. Ladwig, L. Hall and D. Wilson, *Queen's University*

Background: The positive illusory bias is the disparity between self-report of competence and actual competence, such that an individual's self-reported competence is substantially higher than their actual competence. Children with ADHD strongly overestimate their competency relative to external indices such as adult report or actual performance. This overestimation has been linked to conduct problems and aggression over time. A similar bias has also been found in ASD. Individuals with ASD have been found to self-report greater levels of social competence compared to parental-reports and underestimate their autism-related symptoms. Studies have examined self-perceptions by comparing higher-order global questionnaires, to parental reports. There may be problems with this methodology due to parental biases and the difficulty that individuals with ASD have with higher-order concepts and mental states.

Objectives: To extend research on the self-perceptions held by atypical populations by using performance on a specific task as the basis for ratings, rather than a more global measure of overall competency. The study also examines how IQ and executive functioning relate to self-perceptions.

Methods: We anticipate 40 participants, aged 11-18 years, in each of the groups; typical controls, ADHD and ASD ($N = 120$). Currently we have two groups matched on mental age: 7 ASD (6 males, 1 female; *mean age* = 15.5, *SD* = 2.22) and 19 TD (10 males, 9 females; *mean age* = 14.05, *SD* = 1.81) ($N = 26$). Participants are administered the *Autism Diagnostic Observation Schedule* to confirm diagnosis, the *Delis-Kaplan Executive Function System* to measure executive functioning and the *Wechsler Abbreviated Scale of Intelligence* to measure IQ. To test self-perceptions, a verbal and a mathematic task have been derived from *Woodcock Johnson III Tests of*

Achievement. Participants are asked about how well they think they will do before they complete each task (pre-task prediction), how well they think they did after they complete each task (current post-performance rating) and how well they think they will do if they did each task again (future post-performance rating).

Results: Preliminary findings indicate trends that support our hypotheses. Discrepancy scores were used for analyses, where the participant's perceived score is subtracted from their actual score. Mann-Whitney *U* tests evaluated group differences in discrepancy scores. The results of all the tests were in the expected direction, with the ASD group having larger average discrepancy scores than typically developing controls. Both the current and future post-task math questions were significant at the $p < .05$ levels. Correlations were computed to examine the relations between IQ and executive functioning with discrepancy scores. Preliminary analyses suggest a negative relationship between self-perceptions and IQ; however, there seems to be no relationship between self-perceptions and executive functioning.

Conclusions: The data suggest that individuals with ASD have less accurate self-perceptions than TD controls. More accurate self-perceptions tend to be associated with higher IQ scores. We expect to find more conclusive results once more participants have been tested. Examining the positive illusory bias in ASD using pre/post task questions will further our understanding of the causal mechanisms underlying this phenomenon.

164.170 170 Sensory Processing Disorders Patterns in Children with Autism Spectrum Disorders. M. N. Simard*¹, M. Couture², E. Gisel³, E. Fombonne⁴ and C. Kirby⁵, (1)*CHUQ Research Center*, (2)*Centre de recherche Etienne LeBel*, (3)*McGill University*, (4)*Montreal Children's Hospital*, (5)*Université Laval*

Background: Sensory processing disorders have been identified in cohorts of children with autism spectrum disorder (ASD) in many recent studies. According to these studies, between 45% and 95% of children with ASD have sensory processing abnormalities. These difficulties can be defined as dysfunctions occurring during the processing of discrimination, interpretation, modulation and organization of sensory stimulations in the central nervous system.

Processing disorders can affect all sensory systems, i.e. the auditory, visual, vestibular, touch and oral systems. Moreover, according to the theoretical model of neurological threshold and behavioral responses proposed by Dunn, children's responsivity to the perceived stimuli can be classified into the following quadrants: poor registration, sensation seeking, sensitivity to stimuli and sensation avoiding. Despite the high prevalence of sensory processing disorders in children with ASD, the existence of homogeneous or typical portraits of sensory disorders in this population is still pending.

Objectives: To explore the existence of sensory processing patterns in a cohort of children with ASD.

Methods: One hundred and forty-one children diagnosed with ASD and aged between 4 and 7 years old were recruited and assessed with the *Sensory Profile*. The *Sensory Profile* aims to measure the sensory processing abilities and their effect on functional performance in the child's daily living. It is one of the most recognized and used tool for the assessment of sensory processing. Children's results can be analyzed and interpreted according to 2 types of classification: the sensory systems and Dunn's quadrants. Parents of the children with ASD completed the questionnaire and scoring was done by an occupational therapist. Latent class analyses were then conducted with children's results on both types of classification (sensory systems and Dunn's quadrants) to determine the existence of sensory processing disorders patterns.

Results: For both types of classification, two patterns have been identified. According to the sensory systems, children presenting the first pattern (35.3%) are at high risk of sensory disorders in all systems except for the visual domain (*auditive* 0.914 *visual* 0.546 *balance* 1.000 *tactile* 0.937 *oral* 0.828) while children in the second pattern (64.7%) are at low risk of sensory disorders in all systems (*auditive* 0.440 *visual* 0.147 *balance* 0.320 *tactile* 0.396 *oral* 0.399). According to Dunn's quadrants classification, children with the first pattern (76.1%) are at high risk of having all types of responses to perceived stimuli (*sensation seeking* 0.838 *poor registration* 0.747 *sensation avoiding* 0.789 *sensitivity to stimuli* 0.809) while the

children with the second pattern (23.9%) have low risk of showing any types (*sensation seeking* 0.378 *poor registration* 0.140 *sensation avoiding* 0.000 *sensitivity to stimuli* 0.289). For both analyses, goodness of fit statistics converge together.

Conclusions: For both types of classification, children with ASD seem to divide into two types of sensory processing disorders patterns. In fact, the majority of children with ASD have difficulties in both hyper and hypo responsivity which seem to involve each sensory systems. The current results argue for a new classification of scores or a new interpretation of sensory processing difficulties in children with an ASD.

164.171 171 Synaesthesia in Adults with Autism. D. Johnson*, C. Allison and S. Baron-Cohen, *University of Cambridge*

Background: Case studies and anecdotal reports have suggested a link between autism spectrum disorders (ASDs) and synaesthesia, an idiopathic condition in which stimulation of one sensory modality automatically evokes a perception in an unstimulated modality (e.g., a bell ringing triggers the perception of the color blue). The prevailing neurobiological models of ASD and synaesthesia are similar in their emphasis on atypical neural connectivity, and a genetic study also alluded to an association, linking synaesthesia to a chromosomal region associated with autism. A pilot study by Baron-Cohen et al. found a greater rate of self-reported synaesthesia in autistic people compared to non-autistic people (12.7 and 4%, respectively). The difference between the groups was non-significant, likely due to an underpowered sample.

Objectives: To elucidate the relationship between ASD and synaesthesia through estimating the prevalence of synaesthesia in a larger sample of high-functioning autistic adults (Study 1), and comparing the nature of synaesthesia in synaesthetes with and without autism (Study 2).

Methods: *Study 1-* 2291 adults registered on two volunteer databases were invited to join the study via email. 172 autistic adults and 123 typically developing (typical) adults participated. There were no differences in age. The autistic group was 46% female and the typical group was 70% female. Mean AQ, EQ, and SQ-R scores of both groups fell within the normal ranges for their

respective groups. Eight were excluded for reporting a self-diagnosed ASD. Participants completed online and paper questionnaires that defined synaesthesia, and then assessed experiences through a series of screening items. Conservative criteria were used to determine status. Participants who denied experiencing synaesthesia or had a history of drug use or neurological conditions were considered non-synaesthetes. *Study 2-* Self-reported autistic and typical synaesthetes ($n=31$ and $n=7$, respectively) from Study 1 were included. 29 previously confirmed typical synaesthetes were randomly selected from our database and added to the typical synaesthete group to increase power. 54% of autistic synaesthetes were female compared to 81% of typical synaesthetes. There were no differences in age. Questionnaire responses from both groups were compared.

Results: *Study 1-* The current estimate of synaesthesia prevalence is 4.4%. Based on self-report, we obtained significantly different rates of 5.7 and 18.9% for the typical and autistic groups, respectively ($X^2(1, 287) = 10.68, p < .01, \phi = .19$). *Study 2-* Both groups reported instantaneous percepts, unlearned pairings, and lifelong synaesthesia. Consistent with the literature, colors triggered by sounds and written linguistic stimuli were the most common variants reported by both groups. Autistic synaesthetes reported more changes in percept strength, greater influence of emotions on synaesthesia, and greater visual interference from synaesthesia.

Conclusions: Future studies should confirm these prevalence estimates by verifying self-reports with objective measures (e.g., tests of internal consistency). Discovering a greater rate of synaesthesia in the autistic population might suggest the conditions share neurobiological underpinnings. Even if synaesthesia occurs at the same rate in the typical population, understanding how synaesthetic experiences are manifested in behavior could aid understanding of autistic symptomatology.

164.172 172 The Impact of Problem Behavior On Language Outcomes for Preschool-Aged Children with ASD. A. Gutierrez^{*1}, J. M. Weber¹, D. Coman², A. V. Maharaj¹, D. Bagner¹, M. Alessandri², B. Boyd³, K. Hume⁴, L. D. Johnson⁵, L. A. Sperry⁶ and S. Odom⁷, (1)*Florida International University*, (2)*University of Miami*, (3)*University of North*

Carolina at Chapel Hill, (4)University of North Carolina, Chapel Hill, (5)University of Minnesota, (6)Griffith University/University of Sunshine Coast Australia, (7)University of North Carolina

Background: Problem behavior is a common concern for young children with ASD and other developmental disabilities (Horner, Carr, Strain, Todd, & Reed, 2002) and can interfere with social and academic success (Horner, Diemer, & Brazeau, 1992). While there are numerous studies of behavioral interventions for individuals with ASD and other developmental disabilities, the majority of interventions utilize functional behavioral assessment and environmental modifications to reduce the likelihood of problematic behaviors. There is a need for additional research on the impact problem behavior may have on child outcomes in school settings and on interventions that focus on classroom-based approaches to problem behavior. These issues have great potential to impact educational and developmental outcomes for children with ASD.

Objectives: To investigate the relationship between teacher reports of child problem behavior and language outcomes for preschool children with ASD.

Methods: The sample was comprised of 181 children diagnosed with ASD and 27 teachers who were part of a completed multi-site study comparing different pre-school programs for children with ASD. Participants ranged from 3 to 5 years of age and were followed throughout the school year. Children were administered language assessments (PLS4 and Mullen) at the beginning and end of the school year. Teachers completed the Caregiver Teacher Report Form (CTRF) at the beginning of the school year.

The CTRF is composed of 99 items pertaining to behavioral and emotional problems exhibited either now or in the past 2 months. Teachers were asked to rate the child's behavior on a 3 point Likert scale ('very true or often true', 'somewhat or sometimes true', and 'not true'). The CTRF produces three problem behavior scale scores and seven syndrome subscale scores.

Results: Using hierarchical linear regression, results indicated that teacher ratings on the CTRF

Externalizing behavior scale at the beginning of the year significantly predicted scores on the Mullen receptive subscales at the end of the year ($\beta = -.10$, $t(176) = -2.12$, $p < .05$) when controlling for age, pretest scores and classroom model. The Mullen receptive scores accounted for 68.2% of the variance ($R^2 = 0.68$, $F(4,176) = 94.43$).

Conclusions: Those children whose teachers reported a high number of externalizing behaviors on the CTRF at the beginning of the year showed less language gains as measured by the Mullen receptive scales at the end of the year. Other scores yielded by the CTRF ('total problem behavior' and 'internalizing behaviors') do not influence a child's language acquisition on either the PLS4 or the Mullen. These results suggest that it may be important to develop school-based interventions to address problem behavior for young children with ASD in an effort to eliminate possible barriers to positive outcomes.

164.173 173 Dynamic Visual Search Strategies During Natural Viewing in 12-24 Month-Olds with Autism. S. I. Habayeb*, W. Jones and A. Klin, *Marcus Autism Center, Children's Healthcare of Atlanta & Emory University School of Medicine*

Background: The natural environment of toddlers contains a wide array of competing attentional demands: from other people in motion—talking, gesturing, and interacting—to the physical features of the surrounding world (clothing, toys, furniture). In response, people in general, and toddlers in particular, have only limited attentional resources to deploy. By analyzing how individuals direct those limited resources in pursuit of a goal, we may gain insights into both the goals that guide behavior in particular contexts, and how those goals may differ in young children with autism. In a natural viewing task using dynamic scenes of social interaction, this experimental framework was operationalized by measuring the first fixations following a movie scene cut. Related work with adolescents and school-aged children with autism spectrum disorders (ASD) demonstrated that these individuals were more likely to direct their fixations to body and object areas than to the face, while their typically-developing (TD) peers were significantly more likely to shift their first fixations to the eyes of onscreen actors. In younger children, results indicated that TD toddlers were more likely than children with ASD

to shift their attention to the eyes after a scene cut.

Objectives: To understand differences between toddlers with and without ASD in the rapid deployment of initial fixations when presented with new visual information, and to understand how these initial fixations relate to subsequent fixations as well as to sustained looking preferences that persist throughout an entire viewing period.

Methods: Children with ASD and age- and non-verbal IQ-matched TD controls, between the ages of 12-24 months, watched dynamic social scenes of young children playing. Scene cuts provided instances where new visual information required a viewer to shift attention from an old location (in the previous frame) to a new target location (in the current frame). Eye-tracking technology was used to collect visual scanning and fixation data. Dependent measures included reaction times to shift gaze following a movie scene cut; location of first, second, and third fixations within the scene following a cut; overall fixation time spent looking at different regions; and rate of convergence on a new location.

Results: Preliminary results suggests that while reaction times to shift visual attention following a change in visual information are similar between-groups, TD children are more likely to direct their first fixation towards the eyes of on-screen actors than their peers with ASD. Results also show that initial fixation patterns in children with ASD are very highly correlated with overall fixation patterns, whereas visual search strategies vary between initial fixations and subsequent fixations in TD children, suggesting that the gaze strategies of TD children are more strongly modulated by scene context.

Conclusions: This study explores how the analysis of initial fixations may serve as a proxy for 'social intuition' (the first reactions that guide behavior in novel situations) and how ongoing deployment of visual resources varies as novel visual information is presented and as content and contextual cues change over time.

Wang^{*3}, (1)Beijing Normal University, (2)Yan Shan University, (3)Nankai University

Background:

Rapid progress in robotics offers tremendous possibilities for innovation in training for individuals with ASDs. Humanoid robots show potential in this regard because they are predictable, simple and easy to comprehend (Nadel, 2004) and they can be designed in accordance of the particular interests and comprehension deficits of children with ASDs. However, the efficacy and effectiveness research on this topic is in its infancy.

Objectives:

The objective of this study is to investigate how a humanoid robot NAO (Aldebaran-Robotics) can, by appearing more predictable, appealing and simple than a human being, facilitate social interaction skills of kids with ASDs over a period of several months.

Methods:

Four children with ASDs age 5-10 from special education unit at Small World School in Tianjin, China, were selected to participate in the investigation. The NAO robot was connected to a laptop and placed on the floor in a quiet and light room at school. One investigator controlled the laptop in a remote area when necessary and another investigator or teacher was sitting in the room just in case the child needed help. Each trial lasted as long as the child was comfortable with staying in the room. The cameras operated by a remote control. Each child participated in as many trials as possible during a period of four months, with an average of thirty-two trials each. The trials were designed to progressively move from very simple exposure to the robot to more complex opportunities for interaction, such as, eye-gazing, touching, waving hands, repeating, imitating, etc.

Results:

Based on the video material documenting the interactions, a quantitative and qualitative analysis was conducted. Some elementary

behaviour criteria (such as eye-gaze, touch, pointing, social smile, attending to sounds, following instructions, etc.) were defined in our trials that were evaluated throughout the period of trials. The four children with ASDs all showed improvement in their social interaction skills after the trials for four months based on the frequency and duration of the basic behaviours, for instance, they tended to help NAO when he fell over, but had no response when it happened on human beings. The children realized when they made a mistake in imitation and corrected themselves. In some cases, the children used the robot as a mediator, an object of shared attention, for their interaction with other human beings.

Conclusions:

This study presented a longitudinal investigation on the exposure of children with ASDs to a humanoid robot. The findings clearly demonstrate the need for, and benefits of, long-term studies in order to reveal the full potential of humanoid robots in the therapy and education of children with ASDs.

164.175 175 Can Mindfulness-Based Therapy Reduce Executive Impairment in Adults with Autism Spectrum Disorders (ASD)? A. A. Spek*¹ and N. van Ham², (1)*Mental Health Institution Eindhoven*, (2)*GGZ Eindhoven*

Background:

Executive functioning describes a set of processes involved in complex, goal directed actions. Impairment in executive functioning is one of the core deficits in autism. In adults with autism specifically, executive function deficits have been predominantly reported in the areas of cognitive flexibility, planning and working memory. Treatment opportunities for executive problems in adults with ASD are limited and lack scientific proof. Mindfulness-based therapy (MBT) is a relatively new form of treatment that has been proven effective in reducing executive impairment in various disorder groups. MBT has been examined in adults with ASD and results showed a reduction in symptoms of depression and anxiety (Spek, in press).

Objectives: To conduct a preliminary trial in order to examine whether MBT may be effective in

reducing executive impairment in adults with ASD.

Methods: 9 adults with ASD and full scale IQ > 85, received 9 weekly MBT sessions. Diagnoses of the participants were based on the ADI-R and an interview based on DSM-IV criteria of ASD. Executive functioning was examined before and after the intervention, using the Behavior Rating Inventory of Executive Dysfunction (BRIEF).

Results: Data were analyzed and a significant reduction of impairment was found in inhibition, shifting, emotional control, initiate, working memory, planning/organizing and organization of materials. No changes were found for self-monitoring and task monitoring. In October 2012, results of a third measurement (four months after the intervention) will be added.

Conclusions: The results seem to indicate that MBT may be helpful for adults with ASD in reducing executive impairment. We advice further research, incorporating a larger number of participants and a control group.

164.176 176 Internet-Based Support and Coaching for Adolescents and Young Adults with Neuropsychiatric Disorders – a Follow-up of an Intervention from an Organizational Studies Perspective. N. M. Gillberg*¹ and E. Wentz², (1)*Gillberg Neuropsychiatry Centre*, (2)*Institute of Neurosciences and Physiology*

Background: In a pilot study, internet-based support with a personal coach was offered to adolescents and young adults with autism spectrum disorder and/or ADHD. This article summarizes the evaluation of the trial from an organizational perspective, focusing on future implementation of the intervention.

Objectives: Difficulty with social interaction is a trait shared by many neuropsychiatric patients. Particularly face-to-face communication can be problematic. Significant initiation difficulties and impairments in executive function can further complicate visits at clinics i.e. traditional treatment. Internet presents an opportunity to design support measures to a group of patients who often find face-to-face meetings in a clinic stressful. The aims of the project were 1) to develop a model for internet-based support and coaching for adolescents and young adults with

neuropsychiatric disorders (NPD) and 2) to validate the model. Upon completion of the trial, the intervention was evaluated by the participants. The evaluation of the intervention showed improvement of the participants' self-esteem and sense of coherence, indicating that the internet-based support and coaching can be an important complement to other interventions for young people with ASD and/or ADHD.

Methods: The organizational evaluation consisted of semi-structured group interviews with coaches and project managers at the three treatment units involved in the study. Guided by existing implementation research and the collected data, the intervention was evaluated from the following parameters: 1) whether the method could be said to have relative advantages to other methods 2) to what degree the method is in keeping with the values, norms and work practices at the implementation sites 3) how easy the method is to use and 4) to what degree the method could be adapted to local conditions and recipients' needs.

Results: It was concluded that the intervention had quantitative and qualitative advantages relative to other interventions. Organizational culture posed a problem as the intervention was met by negative attitudes among some staff. Insufficient awareness was identified as another issue compromising successful implementation. Gate-keepers on treatment entry levels and management were identified as two groups of key importance to successful implementation. Technical difficulties were reported to affect the quality of the intervention negatively.

Conclusions: The intervention has benefits in terms of both quantity (by reaching individuals that would otherwise not receive any support) and quality (by providing a qualitatively better suited intervention to a group for which traditional interventions are less well suited). The intervention also meets goals of achieving a high level of equality in the patient-caregiver relationship. Further work on staff awareness and attitudes in relation to the intervention will be needed for future implementation of the intervention. Technical issues will also have to be addressed.

Bahrami*, A. Movahedi, M. Marandi and A. Abedi,
University of Isfahan

Background: Stereotypy is one of three core diagnostic features of children with autism spectrum disorders (ASD).

Objectives: The purpose of the present study was to investigate the effects of 14 weeks of Kata techniques on stereotypic behaviors of children with ASD.

Methods: The study included 30 eligible (diagnosed ASD, school age) children with ages ranging from 5 to 16 years whom they assigned to an exercise (n=15) or a no-exercise control group (n=15). Participants of the exercise group received Kata techniques instruction four times per week for 14 weeks (56 sessions). We used the stereotypy subscale of Gilliam Autism Rating Scale- Second Edition (GARS-2) to assess stereotypy severity at baseline (pre-intervention), week 14 (post-intervention), and at one month follow up in both groups.

Results: Kata techniques significantly reduced stereotypy severity in the exercise group. Following participation in Kata techniques training, stereotypy decreased from baseline levels by a M of 42.54% across participants. After 30 days of no practice, stereotypy in the exercise group remained significantly decreased compared to pre-intervention time. The participants of the control group did not show significant changes in the stereotypy severity.

Conclusions: The findings of the present investigation indicate that teaching Kata techniques to children with ASD for a long period of time consistently decreases their stereotypic behaviors.

165 Parent Training and Parent Mediated Intervention in Diverse Contexts

Moderator: M. Yeargin-Allsopp CDC

Organizer: M. Yeargin-Allsopp Centers for Disease Control and Prevention

As awareness of ASD and diagnosis continues to grow globally, an unprecedented number of parents are in search of services for their children. In the absence of formal teacher training programs and experienced professionals, let alone evidence-based programs, parent training and parent mediated intervention play a critically important role in intervention for families who may otherwise have limited

options. The basic components of parent-focused training often overlap, including the content covered, methods, and intended outcomes. However, the challenge is to either identify interventions or combine aspects of intervention that address local needs, have social validity, and are feasible in different settings-- including in low and middle income countries (LMIC) and underresourced settings. In this symposium, we present approaches to parent training at three stages of development and from six diverse settings: exploration of parent needs in a remote part of Morocco; adaptation and implementation of Responsive Teaching and applied behavior analysis in Turkey, Poland, and Mexico; and evaluation of a model focused on parent empowerment and acceptance in India. Each presentation will outline the rationale behind the approach, structure of the program, and will discuss lessons learned that inform parent training across a broad context and with diverse populations.

165.001 Working with Parents: A Pilot Project in Southern Morocco. M. V. de Jonge*¹, S. Klok-van Reedt Dortland², S. Arbib³ and E. Stallen⁴, (1)*Rudolf Magnus Institute of Neuroscience, University Medical Center Utrecht*, (2)*School Cooperation*, (3)*N/A*, (4)*Psychology Practice*

Background:

The importance of studying autism in non-western countries has been emphasized in recent years (Grinker et al., 2012; WHO, 2008). A considerable number of epidemiological surveys already have been carried out (Elsabbagh et al., 2012). As in Western countries, many of these studies tried to identify children with ASD at an early age. Notwithstanding the apparent significance of the efforts to estimate the prevalence throughout the world and to detect ASD early in life, some question the utility and ethics of early diagnosis in areas with limited resources and services. Others question whether research efforts should focus on ASD only or should incorporate a wider range of developmental disorders.

Objectives:

This paper presents the results of a pilot project undertaken in cooperation with parents in the southern part of Morocco. The goal was to jointly determine an effective way to empower parents of children with developmental disorders, a group who often have no access to day care or school.

Methods:

In cooperation with a parent organization in Ouarzazate (south Morocco) we explored the needs and questions of parents of children with

developmental disorders. Additionally, we organized a three-week pilot summer program for a small group of children with developmental disorders, their parents and volunteers. During this period, we undertook several steps to explore parent needs by 1) exchanging knowledge about autism and developmental disorders and provided diagnostic evaluations; 2) worked out individual plans for the children in collaboration with parents and local volunteers; and 3) worked with children and parents in order to model interventions and educational strategies. During this period we trained local volunteers from the parent organization to monitor the individual plans and to support the parents. Two follow-up visits are planned.

Results:

Seven children with developmental disorders and their mothers took part in this pilot project. Four volunteers from the Netherlands (three child psychologists, one educational assistant) worked together with four Moroccan volunteers. In addition three information meetings were organized in collaboration with local health care workers for parents, teachers and stakeholders. We encountered both success and challenges. Some of our original goals did not match the needs and questions of the parents. For instance, fewer parents of children with autism were interested in participation than anticipated, while parents of children with other developmental disorders were very keen to take part. Also, parents of young children with were very reluctant to participate, while there was a strong request for support of parents with older children.

Conclusions:

Despite the challenges, the pilot project was highly valued both by parents and volunteers from both countries. During the presentation, we will outline the benefits and the pitfalls of this pilot project. Lessons learned for this project and other parent intervention projects in underserved non-western regions will be discussed. Finally, we will discuss possible benefits of this project for the Moroccan immigrant population in the Netherlands.

165.002 Adopt or Adapt? Working with Parents to Facilitate Implementation of Evidence-Based Strategies in Turkey, Poland and Mexico. L. J. Hall*¹ and O. Karaaslan², (1)*San Diego State University*, (2)*Marmara University*

Background:

A review of comprehensive treatment models revealed that there are parent mediated models and those with parent training components that have published research evidence of effectiveness for the model as a whole, or for key focused interventions that define the model (Odom, Boyd, Hall, & Hume, 2010). It is understandable that interventionists and families of individuals with ASD living around the globe would want to implement those models and strategies that are evidence-based. There is a lack of information about how to effectively implement and adapt effective practices when the cultural context differs from the one in which the model was developed. Through an analysis of four examples of the effective implementation of three different models in 3 countries (Turkey, Poland & Mexico) we can gain a better understanding of how to effectively adopt (work with families to overcome cultural barriers to implementing key strategies) and adapt (make changes in strategies so they can be used effectively in the cultural context) evidence-based parent mediated and parent training approaches.

Objectives:

This presentation will 1) describe examples of both adopting and adapting key features of evidence-based strategies when working with families in three countries (Turkey, Poland, and Mexico) and 2) summarize the similarities of strategies used to adopt and adapt practices across contexts.

Methods:

Information for this qualitative study was obtained through open-ended interviews with model developers of select comprehensive treatment models (Responsive Teaching, Princeton Child Development Institute, & Lovaas Institute) that include parent training. The models represent a clinic-based parent mediated approach, parent training accomplished in groups in a clinic and school, and individualized, home-based parent

training. Implementers of these models in Turkey (Responsive Teaching & PCDI), Poland (PCDI) and Mexico (Lovaas) were interviewed, and asked to provide examples of how they worked with families to adopt these key features to the cultural context and how they adapted program features to fit the cultural contexts. Interview results were evaluated for similarities and differences in these examples across contexts.

Results:

Across contexts implementers were reluctant to adapt key model features due to concerns about jeopardizing the integrity of the program and, consequently, the effectiveness of the strategies for families and their children with ASD. Implementers of the strategies all provided examples of how they worked with families to facilitate the adoption of strategies that initially were not supported or uncomfortable for the families. They also all adapted those practices that were not seen as critical to the model or adapted features in a way that did not change the critical features of the strategy.

Conclusions:

Evidence-based strategies were successfully used and adopted in various cultural contexts in spite of initial concerns by model implementers and families about lack of cultural congruency. Implementers were very creative and highly skilled at problem-solving when challenges were presented. Examples of how strategies were adopted and adapted will inform those working in other countries that plan to use such evidence-based practices with families.

165.003 Evaluation of an Acceptance and Empowerment Parent Training Model: Evidence From India. T. C. Daley*¹, N. Singhal², T. S. Weisner³, M. Barua² and R. S. Brezis³, (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. Moreover, even when children attend schools, 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 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 350 participants.

Objectives:

This study first describes the theoretical underpinnings of this community-based parent-training model, and presents a multi-method evaluation undertaken to understand it. The study itself is a partnership between the UCLA Culture, Brain, Development and Mental Health program, and a nongovernmental organization in India, Action For Autism.

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 and mothers attended the program. Measures consisted of a combination of standardized tools and those developed specifically for this evaluation under a broader project on research on families with autism in India. Parents and children are followed six and 12 months after the conclusion of the PCTP program. In addition to pre-post comparisons, the subsequent cohort served as a non-treatment comparison at the post-test to guard against selected threats to internal validity.

Results:

Cohorts did not differ in demographic characteristics or baseline outcome measures. Significant gains were seen across all outcome measures, including parents' empowerment, acceptance, knowledge of autism, sense of competence, and stress. Post-test scores on these measures were significantly higher than the equivalent comparison group.

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. The acceptance and empowerment focus of this model offers a novel way to conceptualize parent training, and has high relevance for families in situations where cultural, economic and other contextual factors may be similar to those in India. Lastly, this study suggests that existing intervention models may offer critically important information for researchers interested in testing or examining programs developed in other settings.

165.004 Discussant. A. Stahmer*, *Rady Children's Hospital, San Diego*

Background:

N/A

Objectives:

N/A

Methods:

N/A

Results:

N/A

Conclusions:

N/A

Cognition and Behavior Program

166 Novel Perspectives On the ASD Phenotype

166.001 Towards a Core Outcome Set for Young Children with Autism Spectrum Disorder. H. McConachie*¹, N. Livingstone², C. Morris³, B. Beresford⁴, A. S. Le Couteur⁵, P. Gringras⁶, D. A. Garland⁷, J. Parr⁸, G. Jones⁹, G. Macdonald² and K. Williams¹⁰, (1)University of Newcastle, (2)Queen's University Belfast, (3)University of Exeter, (4)University of York, (5)Newcastle University, (6)Kings College London, (7)National Autistic Society, (8)Institute of Neuroscience, Newcastle University, (9)University of Birmingham, (10)University of Melbourne and Royal Children's Hospital

Background:

Young children with autism spectrum disorder (ASD) have widely varying abilities and severity of difficulties. There is some evidence that early interventions are effective in helping children to develop and progress, and improve family quality of life.

One problem for researchers and service providers is the multitude of measurement tools used to collect evidence about children's development. These include communication, skills, ASD characteristics, behaviours such as faddy eating, sleep problems and sensory issues, and ways of observing children's social skills. We do not know whether such tools match parents' priorities for their children's progress, nor whether teachers and other professionals find them useful.

Objectives:

To present a consultation and review process leading to proposals on what outcomes it is important to measure when monitoring progress of young children with ASD.

Methods:

The research team includes ASD experts and review methodologists. We conducted a review of qualitative literature to explore parents' priorities for their children with ASD. Direct consultation was with three parent advisory groups in different parts of UK; and a survey of over 700 professionals working with children with ASD asking what outcomes they currently measure.

The process draws on recommendations of COMET (*Core-Outcome-Measures-in-*

Effectiveness-Trials, <http://www.comet-initiative.org/>) which advises on the development and application of agreed standardised sets of outcomes.

Results:

More than sixty possible outcomes extracted from the three sources of information were entered into a conceptual framework drawn from the International Classification of Functioning, Disability and Health, i.e. into domains of 'impairments', 'activity limitations', 'participation restrictions', and family measures. The parent groups' rating of the most important outcomes bears little relationship to what professionals most often measure.

Conclusions:

The contrast between what parents consider important outcomes and what professionals actually measure highlights the importance of using a multi-faceted process to reach consensus. This consultation about WHAT to measure is the first stage in a systematic review of the quality and appropriateness of tools to monitor children's progress and outcomes, commissioned by the UK National Institute for Health Research. The next stage will be to systematically search literature about HOW outcomes are measured and review all available evidence about the most robust measurement tools. Finally we will draw up consensus recommendations of a set of tools, with input from parents, to be used in future by researchers and service providers.

This presentation describes evidence synthesis commissioned by the National Institute for Health Research (NIHR) under the Health Technology Assessment programme (HTA Project:11/22/03). The views expressed are those of the authors and not necessarily those of the National Health Service, NIHR or Department of Health.

166.002 Linguistic Strengths and Weaknesses in Optimal Outcome Children with a History of Autism Spectrum Disorders. L. Naigles*¹, J. Suh¹, I. M. Eigsti¹, E. A. Kelley², A. Orinstein¹, K. E. Tyson¹, E. Troyb¹, M. Barton¹ and D. A. Fein¹, (1)University of Connecticut, (2)Queen's University

Background:

Children with Autism Spectrum Disorders (ASDs) exhibit symptoms that, historically, have been considered part of a lifelong disorder. A growing body of research indicates that, through intensive early intervention, children with ASDs may show notably reduced problems in language, cognition, and social interaction and may even lose their ASD diagnosis (Harris & Handleman, 2000; Kelley, Paul, Fein, & Naigles, 2006). Kelley et al. (2006, 2010) have reported some residual linguistic weaknesses in such optimal outcome (OO) children at 7-10 years of age; however, comprehensive assessments of the language abilities of OO adolescents are needed, especially using both standardized and psycholinguistic tests.

Objectives:

The current study examines the language of OO adolescents, who were diagnosed with ASD before age 5, but who no longer meet criteria for an ASD diagnosis and are placed in mainstream classrooms. Their language is compared to group with age-matched individuals with high-functioning autism (HFA) and typically developing individuals (TD).

Methods:

Participants include TD children and adolescents (mean age = 13.23), children and adolescents with high-functioning autism (HFA) (mean age = 13.18), and OO children and adolescents (mean age = 12.91). Group Ns varied depending on the task; all Ns >15. Groups did not differ in NVIQ ($p > .4$). Children participated in standardized tests, including Comprehensive Evaluation of Language Fundamentals (CELF), Peabody Picture Vocabulary Test (PPVT), Comprehensive Test of Phonological Processing (CTOPP), Test of Language Competence (TLC) and a narrative elicitation task (Tuesday Story from the ADOS).

Results:

The OO group had significantly lower scores than the TD group on the formulated sentences subscale of the CELF; all other standardized test measures yielded no TD/OO group differences. The HFA group had significantly lower scores than the TD group on the CELF, PPVT, CTOPP, and TLC,

and performed worse than the OO group on the CELF and TLC. On the narrative task, the OO and HFA groups produced more dysfluencies and idiosyncratic language than the TD group. HFA (but not OO) children also produced more ambiguous pronouns and fewer story elements than the TD group.

Conclusions:

The HFA participants continued to show a range of receptive, expressive, and pragmatic deficits. Overall, the Optimal Outcome children showed remarkably good language abilities. Residual difficulties relative to the TD group were observed only with subtle expressive skills, including creating new sentences and showing mild disfluencies in telling stories. The use of ambiguous pronouns, however, which arguably reflects failure to take the perspective of the listener, was elevated in the HFA but not the OO group, suggesting that this aspect of pragmatics has reached normal levels in the OO group.

166.003 Compromised Quality of Life in Autism Spectrum Disorders. A Case-Controlled Long-Term Follow-up Study, Comparing Young High-Functioning Adults with Autism Spectrum Disorders with Adults with Other Psychiatric Disorders Diagnosed in Childhood. H. Swaab¹, P. S. Barneveld^{*1}, S. Fagel¹, H. van Engeland² and L. M. J. de Sonneville¹, (1)*Leiden University, Faculty of Social Sciences*, (2)*University Medical Centre Utrecht*

Background: Children with autism spectrum disorders (ASD) are characterized by marked impairments in social interaction and communication, and these deficiencies increasingly hamper daily life functioning as demands for social relationships and independent living become larger and more prominent when growing older. Reviews of quality of life (QoL) in adulthood indicate that the prognosis of ASD is generally poor; a minority of individuals with ASD live independently, few individuals have social and intimate relationships, and education and employment levels are low, even when general intelligence is within the normal range. Since ASD is a condition in which there is a profound impairment in social adaptation in adulthood, it can be expected that the QoL of individuals with ASD is worse compared to the QoL of individuals with other child psychiatric disorders. This study is about specificity, i.e., about comparison of QoL

between young adult psychiatric patients that were diagnosed in childhood or adolescence.

Objectives: Long term outcome in childhood ASD was evaluated by studying QoL in young adulthood in comparison to the outcome of other child psychiatric disorders.

Methods: In this follow-up study, objective and subjective QoL of 169 high-functioning adults with ASD (19 to 30 years) was contrasted with QoL data of age matched adults diagnosed with attention deficit/hyperactivity disorder ($N=85$), disruptive behaviour disorders ($N=83$), and affective disorders ($N=85$) diagnosed during childhood. The mean follow-up period of the ASD patients was 13.9 years. Objective QoL included marital status, living arrangements, level of education, employment, and usage of mental health care. Subjective QoL included satisfaction concerning living arrangements, work or education, physical condition, partner relationship, social relationships, state of mind, and future perspective.

Results: QoL was more compromised in adults diagnosed with ASD in childhood than in adults with other psychiatric disorders in childhood. A relatively large proportion of the adults with ASD were single, few lived with a partner or a family and many of them were institutionalized. Adults with ASD had lower educational levels, relatively few had paid employment and many were social security recipients, as compared to the other psychiatric patients. In case the adults with ASD used medication, 47% used anti-psychotics. Regarding the subjective QoL, the adults with ASD were less satisfied about their work or education, partner relationship, and future perspective than the other groups. Even when highly educated adults with ASD were compared to highly educated adults diagnosed with other childhood disorders, the QoL appeared to be more disadvantageous in adults with ASD.

Conclusions: Many studies have shown that QoL is challenged in psychiatric patients, but findings of this study indicate that young high-functioning adults diagnosed with ASD in childhood are at relatively high risk for poor QoL compared to other childhood psychiatric disorders.

166.004 The Role of Language in Social Cognition Among Children with HFASD, LD, and Typ: Social Information Processing, Executive Function, and Theory of Mind. N. Bauminger*, Bar-Ilan University

Background:

Background: The heart of social-cognitive understanding of social situations lies in adequate social information processing (SIP), through which children encode social cues, provide interpretations for encoded stimuli, search for possible social responses, evaluate responses' social appropriateness, and choose the best solution for enactment. Two related capabilities are required to enable efficient SIP: mentalizing other minds (theory of mind – ToM) including others' thoughts, feelings, desires, and intentions; and executive-function (EF) capabilities like planning and cognitive flexibility. Although not extensively examined in clinical populations, SIP, ToM, and EF alike are not intact in children with high-functioning autism spectrum disorders (HFASD) or with learning disabilities (LD), which seriously impedes their social functioning compared to children with typical development (TYP). However, prior research did not compare HFASD and LD or examine the links between SIP, ToM, and EF, nor was the role of language determined.

Objectives:

Objectives: This novel study is aimed at providing comprehensive understanding of the unique socio-cognitive profile of each clinical population (HFASD, LD) by comparing the two and comparing them to children with TYP, while controlling for language differences, as well as by examining links between SIP, ToM, and EF.

Methods:

Method: Study participants included 96 boys in Grades 3-6 matched on CA, comprising 33 TYP, 38 LD, and 25 HFASD. Measures included Crick and Dodge's (1994) SIP scale; EF tasks measuring planning (*Tower of Hanoi*, Borys, Spitz, & Dorans, 1982) and cognitive flexibility (*D-KEFs*, Delis, Kaplan, & Kramer, 2001); and a ToM task (*Faux Pas Stories*, Baron-Cohen, O'Riordan, Stone, Jones, & Plaisted, 1999). Language was controlled via a nationally-normed language test (*Mashe*,

Rom, Morag, & Peleg, 2007) providing a comprehensive language assessment and language-age score.

Results:

Results: Before controlling for language results demonstrated that the HFASD group showed the lowest SIP, EF, and ToM capabilities compared with both LD and TYP peers. More specifically, SIP coding and response generation were lower than TYP in both LD and HFASD, but HFASD also had difficulties in cue interpretation and goal clarification and were lowest in generating effective responses. On EF tasks, both clinical groups were lower than TYP in planning as well as cognitive flexibility during self-sorting. But on the EF cognitive-flexibility task of categorization and its explanation, the HFASD group was lowest, TYP was highest, and LD was in between. On ToM skills, again the HFASD group was lowest.

Controlling for groups' language differences canceled out group differences in most SIP steps as well as in EF-planning, but differences in EF-cognitive-flexibility and ToM remained. SIP was found to correlate with both EF and ToM in the entire study population, attesting to their importance for SIP; however, Z-Fisher tests to examine the significance of differences in correlations between groups did not reveal a homogeneous profile.

Conclusions:

Conclusions: This study's findings broaden understanding of social cognition in HFASD and LD and emphasize the role of language in socio-cognitive skills. SIP, ToM, and EF seem most vulnerable in children with HFASD. Implications for intervention are discussed.

166.005 Making Sense of Repetitive Behaviours in Autism Spectrum Disorder: The Relevance of Intolerance of Uncertainty. J. Rodgers^{*1}, S. Wigham², L. Gray¹, E. Honey¹, M. H. Freeston¹, S. R. Leekam³ and M. South⁴, (1)*Newcastle University*, (2)*Newcastle University Institute of Health and Society*, (3)*School of Psychology, Cardiff University*, (4)*Brigham Young University*

Background: Restricted and repetitive behaviours (RRB) are a hallmark feature of Autism Spectrum Disorder (ASD), although a clear

understanding of the relationship between RRB and other features of ASD is yet to be developed. Difficulties managing sensory input and the presence of anxiety have both been associated with higher levels of RRB in young children with ASD (Chen, Rodgers & McConachie 2009; Rodgers, et al., 2012). The mechanism via which these two constructs may contribute to the presence of RRB has not been fully explored. The construct of intolerance of uncertainty (IU; Dugas et al., 1998) is used here to attempt to bridge this divide. Intolerance of uncertainty is an assumption that uncertainty is stressful and upsetting and unexpected events are negative and should be avoided at all costs. It is hypothesised that intolerance of uncertainty may make a significant contribution to the relationship between sensory sensitivities anxiety and RRB in ASD.

Objectives: To examine the contribution of sensory sensitivities, anxiety and intolerance of uncertainty to the presence of RRB.

Methods: Parents of 23 young people with a diagnosis of ASD, aged between 8-15 years, completed the Spence Children's Anxiety Scale – Parent version (SCAS-P); the Intolerance of Uncertainty Scale Parent version (IUS-P); the Repetitive Behaviour Questionnaire (RBQ) and the Short Sensory Profile (SSP).

Results: Total RBQ score correlated with total SSP score ($r = -.39, p = .021$), total SCAS-P score ($r = .52, p = .005$) and total IUS-P score ($r = .61, p = .001$).

To explore the relationship between sensory sensitivities, anxiety and IU in predicting RRB a hierarchical regression model was built. SSP total score entered at Step 1 was marginally significant in predicting RRB ($\beta = -.15, p = .06$), when total SCAS-P score was entered at Step 2 it was a significant predictor of RRB ($\beta = .27, p = .02$), whilst the contribution of sensory sensitivities was reduced ($\beta = -.10, p = .15$). IUS-P total score entered at Step 3 further reduced the contribution of both sensory sensitivities ($\beta = -.09, p = .15$) and anxiety ($\beta = .15, p = .17$), whilst IU was found to be a significant predictor of RRB ($\beta = .37, p = .02$).

Conclusions: Findings reveal that intolerance of uncertainty may play an important mediating role in the previously reported relationship between sensory sensitivities, RRB and anxiety in children with ASD. Sensory abnormalities present a myriad of challenges for the young person with ASD. Facing such difficulties on a day to day basis may contribute to the development of anxiety which is characterised by intolerance of uncertainty and ultimately circumscribed interests, insistence on sameness, rituals and routines in an attempt to avoid aversive sensory experiences and reduce demand. Recent developments in cognitive behavioural therapy approaches addressing intolerance of uncertainty may hold promise for reducing RRB and anxiety in young people with ASD.

166.006 ASD Is Characterised by Atypicalities in Emotion-Related Learning Processes: What Are the Implications?. S. B. Gaigg* and D. M. Bowler, *City University London*

Background: One of the most robust phenomena in the memory literature is that emotionally salient stimuli are remembered better and for longer than hedonically neutral stimuli. Interactions between the amygdala and the hippocampus are critical for mediating this effect and emotional influences on memory can be dissociated experimentally from other memory phenomena. For instance, Kensinger & Corkin (2004) showed that memories for emotionally arousing stimuli are selectively resistant to the effects of attentional manipulations at encoding. We have previously shown that the long-term retention of emotional material is compromised in ASD (Gaigg & Bowler, 2008) but it remains unclear whether the short-term influences of emotion on memory might be preserved (see Gaigg & Bowler, 2008 and South et al., 2008).

Objectives: Here we draw on the work of Kensinger & Corkin (2004) to test the prediction that the short-term retention of emotional stimuli in ASD is quantitatively preserved but mediated by domain-general memory processes rather than specific mechanisms that are engaged by arousing stimuli (i.e., amygdala-hippocampal interactions). Specifically, we predict that the encoding of arousing words in ASD is not immune to manipulations of attention, as is the case for typically developing (TD) individuals.

Methods: 30 TD and 30 ASD adults, matched on chronological age, gender and verbal ability, participated in the experiment. They were asked to try to remember two lists of words comprising emotionally arousing items (taboos & profanities), hedonically valenced but non-arousing items (e.g., accident, victory,...) and hedonically neutral but categorically related words (items of clothing). Words were presented one at a time on a PC monitor and participants were required to study one list under full-attention and one under divided-attention conditions. During the former, participants studied words without distractions whilst during the latter they were required to monitor a continuous sequence of tones for pitch changes. The order of conditions was counterbalanced and after each list participants wrote down all words they could recall.

Results: Groups performed similarly on the tone monitoring task ($t(58) = .007$, ns) and the free recall results confirmed our predictions. Thus, for the TD group the manipulation of attention affected recall of categorically related and valenced words significantly more than recall of arousing items ($F(1,29) = 5.29$, $p < .05$), confirming that qualitatively different processes are engaged during the encoding of arousing material. In the ASD group, by contrast, there was no indication of such an interaction between attention (full vs. divided) and word type (arousing vs. valenced vs. category) ($F(1,29) = 0.33$, ns).

Conclusions: Together with previous studies, our observations provide clear evidence that emotional learning mechanisms are compromised in ASD, which has significant implications for developmental theory. Most important amongst these is that it forces us to re-consider the widespread assumption that only the social-emotional functions of the amygdala are compromised in ASD. We will argue against social-motivational theories that are based on this assumption and suggest instead that the developmental trajectory of ASD is more fruitfully conceptualised as resulting from a disruption of basic emotion-related learning mechanisms.

166.008 Familiarity of Social Responsiveness Scale Scores in the Nurses' Health Study II. K. Lyall*¹, J. N. Constantino², A. Ascherio³, M. G. Weisskopf³ and S. L. Santangelo³,

(1)University of California, Davis, (2)Washington University School of Medicine, (3)Harvard School of Public Health

Background:

The Social Responsiveness Scale (SRS) is a widely used measure of autistic traits and social functioning. Familiarity of SRS scores has been suggested, but how scores associate with factors related to autism spectrum disorders (ASD) has not been fully examined in large population-based studies.

Objectives:

To examine familiarity of SRS scores, assess associations with child comorbidities, and explore whether adjustment for parent SRS scores, as a measure of underlying genetic susceptibility/broader autism phenotype (BAP), altered associations with certain risk factors for ASD. We also examined whether these factors were related to ASD severity as measured by child SRS scores.

Methods:

Participants were part of a nested case-control study within the Nurses' Health Study II. SRS forms were mailed to participants; mothers (nurse participants) completed child forms and spouses completed parent forms. Familiarity was assessed through Pearson correlation coefficients for parent-child scores and by t-tests comparing child scores according to elevated parent scores (defined as the top 20% of the distribution). Child scores according to maternal report of comorbid neuropsychiatric conditions were compared by t-test. T-tests stratified by case status were used to compare scores based on: demographic factors (education, income, parental age), maternal obesity, gestational diabetes, and depression. Logistic regression was used to obtain estimates of the association between these factors and offspring ASD adjusted for parental SRS scores and other potential confounders.

Results:

470 cases and 1,647 controls returned SRS forms (representing over 70% of the follow-up study). Case fathers had significantly higher SRS scores than control fathers ($p < .0001$). Parent scores were correlated in both cases and controls (r in

total study group = .32), suggesting assortative mating. Child scores were higher for those with parent-reported neuropsychiatric conditions in controls, though still within the normative range; in case children, only maternally-reported comorbid obsessive-compulsive disorder was associated with higher child scores. Parent elevated scores in controls were associated with significantly higher child scores ($p < .0001$) relative to those with parent scores in the lower 80% of the distribution, corresponding to a shift in child raw score of approximately 15 points; the effect was stronger when the father had the elevated score, when the child was male, or when both parent scores were elevated. Elevated scores in case parents were not associated with concordant increases in child scores, though case parents were significantly more likely to have concordantly elevated scores (both parents in top 20% of distribution) than were control parents ($p = 0.0008$). This association persisted in adjusted analyses (odds ratio for parent concordantly elevated scores comparing cases to controls = 2.09, 95% CI 1.22, 3.59). Maternal depression was associated with increased mother and child SRS scores; other factors were not associated with scores. In models adjusting the previously identified risk factors for parental SRS scores associations were somewhat attenuated.

Conclusions:

Our results demonstrate familiarity of autistic traits, as measured by the SRS, and suggest associations in this cohort with previously identified ASD risk factors are not largely impacted by parental BAP.

Treatment Trials: Behavioral Interventions Program

167 Treatments: Medical and Behavioral Trials and Mechanisms

This session presents novel behavioral and medication trials with emphasis on mechanisms.

167.001 Effects of a Targeted Face-Processing Intervention On Visual Attention to Naturalistic Social Scenes. P. Lewis^{*1}, J. M. Moriuchi¹, C. Klaiman¹, J. Wolf², L. Herlihy³, W. Jones¹, A. Klin¹, J. W. Tanaka⁴ and R. T. Schultz⁵, (1)Marcus Autism Center, Children's Healthcare of Atlanta & Emory University School of Medicine, (2)Yale Child Study Center, (3)University of Connecticut, (4)University of Victoria, (5)Children's Hospital of Philadelphia

Background: Children with autism spectrum disorders (ASD), as compared to typically-

developing peers, are selectively impaired in their ability to recognize facial identity. Eye-tracking studies have shown that viewing patterns in children with autism are driven by the physical contingencies of a stimulus rather than its social context. A critical question is thus whether viewing patterns can be enhanced through a direct training intervention.

Objectives: The aims of the current study were (1) to assess the effect of a face-processing intervention on visual attention to dynamic social scenes and (2) to examine the relationship between performance on targeted face-processing tasks and patterns of visual attention to faces within more naturalistic settings.

Methods: In a randomized clinical trial, school-age children diagnosed with ASD were pre-screened with the Let's Face It! skills battery that measures both face and object processing abilities. Participants who were significantly impaired in their face processing abilities were assigned to either a treatment (N=42) or waitlist group (N=37). Children in the treatment group received 20 hours of face training with Let's Face It! (LFI!) computer-based intervention. The LFI! program was composed of seven interactive computer games that targeted specific face processing impairments associated with ASD, including the recognition of identity across image changes in expression, viewpoint, and features, analytic and holistic face processing strategies, and attention to information in the region of the eyes. Children were re-assessed using the LFI! skills battery post-treatment.

In a subset of participants (13 of the children in the treatment group and 15 in the waitlist group), eye-tracking data were collected at both time points while the children viewed videos of children and adults engaged in naturalistic, age-appropriate social interaction. Percentage of visual fixation time on eyes, mouth, body, and object/background regions was calculated across all scenes for each viewing. Time-varying visual scanning patterns were also measured using kernel density estimation. Viewing patterns at Time 1 were compared to those of Time 2, as well to normative viewing patterns from a sample of 36 age- and IQ-matched typically-developing peers.

Results: Preliminary analyses on viewing patterns in a subset of the sample (n=5) suggested an interaction between time point and treatment condition ($\eta_p^2=0.12$). Following LFI! training, children looked more at faces (eyes and mouth regions combined) and less at object/background regions than during pre-training ($d=0.79$). The viewing patterns of children in the waitlist condition changed less across time ($d=0.25$). Ongoing analyses will examine the effect of LFI! training in the full sample, where the greater power will enable evaluation of the statistical significance of these findings. These analyses also will include more detailed study of time-varying visual scanning patterns as well as an investigation of how changes in performance on the LFI! face-processing skills battery may mediate changes in visual attention to the naturalistic stimuli.

Conclusions: The present study suggests that direct face-processing training using the LFI! program alters how children with ASD engage with their natural social visual environment.

167.002 A Psychosexual Training Program for Adolescents with Autism Spectrum Disorder (ASD); The First Effects of the Tackling Teenage Training. K. Visser*¹, L. P. Dekker², E. van der Vegt¹, F. Boudesteijn¹, F. C. Verhulst², A. Maras¹ and K. Greaves-Lord², (1)Yulius, (2)Erasmus MC - Sophia's Childrens Hospital

Background: Adolescents with ASD seem to have similar psychosexual needs to typically developing adolescents, but lack the necessary knowledge and social skills to fulfill these needs (Hénault, 2005; Mehzabin & Stokes, 2011). Therefore, an individual training program was developed in The Netherlands targeting the psychosexual development of adolescents with ASD; the Tackling Teenage (TT) Training. Aims of the training are to increase knowledge, skills, and self-esteem regarding puberty and sexuality and to decrease vulnerability, deviant behaviour and worries of adolescents with ASD. Parents are involved in the training through homework assignments and email contact.

Objectives: To investigate the effect of the Tackling Teenage Training on knowledge, skills, self-esteem, vulnerability, deviant behaviour of adolescents with ASD and worries of parents and adolescents with ASD.

Methods: The TT Training consists of 18 weekly individual sessions with the adolescent and a trained professional. Knowledge of puberty and sexuality (measured with a self-report knowledge test) and psychosexual development, measured with the newly developed Teen Transition Inventory (TTI; self-report and parent-report version) were administered before (T1) and after the training (T2). We conducted a pilot study and are now conducting a *Randomized Controlled Trial* (RCT), with a control condition and an intervention condition ($N = 150$). At this point we have data of a Dutch sample of $n = 74$ at T1 with a mean age of 14.8 years (SD 1.92), mean TIQ 102.9 (SD 12.93), mean SRS total score 102.9 (SD 24.03). 74% of this sample is male. We have T2 data at this point of $n = 21$.

Results: Knowledge regarding puberty and sexuality increased significantly with a mean of 26 correct answers at T1 to a mean of 34 correct answers ($p < 0.001$) at T2. Parents reported a growth in skills in their children, for instance in recognizing boundaries (T1: 0%, T2: 30%, $p < 0.05$). More adolescents reported that they are satisfied with their own bodies (T1: 24%, T2: 71%, $p < 0.05$) and adolescents reported less problems making friends (adolescents T1: 25%, T2: 9%, $p < 0.05$). Generally the worries of parents and adolescents about the future decreased, for instance parents reported to worry less about the vulnerability of their child after the TT training (T1: 67%, T2: 65%, $p < 0.05$). However, parents reported more worries about the future autonomy of the adolescent (T1: 76%, T2: 86%, $p < 0.05$).

Conclusions: The first results show that the TT Training generates a positive outcome regarding knowledge about puberty and sexuality, social skills and worries of parents and adolescents. However, some worries about the future increased. The increase in worries can possibly be explained through better insight in the difficulties of their child. We expect to be able to present the full results of $n = 50$ at the time of the presentation.

167.003 Minimally Verbal Children with ASD: Neural Mechanisms and a Novel Speech Intervention. C. Y. Wan^{*1}, B. Scherrer², J. Chiew¹, J. L. Colet¹ and G. Schlaug¹, (1)*Beth Israel Deaconess Medical Center and Harvard Medical School*, (2)*Children's Hospital Boston*

Background: It has been estimated that up to 30% of children with ASD are minimally verbal or nonverbal, even after receiving years of intensive therapies. However, almost all clinical and neuroimaging studies have focused on the high-functioning, verbal end of the spectrum. As a result, we know almost nothing about why a large portion of children with ASD are nonverbal. This limited knowledge prevents clinicians from testing new therapies and making appropriate treatment recommendations. Over the past few years, our laboratory has developed a novel speech intervention – known as Auditory-Motor Mapping Training (AMMT) – for nonverbal verbal children with ASD. This intervention works by mapping sounds to oral articulatory actions through intonation and bimanual motor activities. Furthermore, the association of sounds with actions engages an auditory-motor network of brain regions, which has been reported to be dysfunctional in ASD, but is of critical importance for developing speech.

Objectives: Here, we report a series of treatment studies that our laboratory has conducted to test the efficacy of AMMT, including a proof-of-concept study, and a randomized controlled trial comparing AMMT to a control treatment (CT). In addition, we report our ongoing neuroimaging research on nonverbal children with ASD, which seeks to understand the neural correlates of nonverbal ASD, as well as to examine whether treatment can change the relevant brain structures.

Methods: All children who participated in our studies were between 4-10 years of age, and had no intelligible words prior to enrollment. They underwent intensive one-on-one AMMT sessions 5 times per week for 5 weeks, and were assessed on their consonant-vowel productions multiple times before, during, and after therapy. In our proof-of-concept study, 6 children participated. In our AMMT vs CT study, 16 children were randomly assigned to receive either AMMT or CT. In CT, the key components of AMMT (intonation and hand-motor actions) were omitted, but the intervention was also designed to promote speech production. In our brain imaging studies, 12 nonverbal children were scanned using DTI, sMRI, and fMRI without sedation. Their brains were compared with those of age-matched typically-developing children.

Results: Results from our treatment studies showed that AMMT resulted in significant improvements in speech production (i.e., increased repertoire of speech sounds and intelligible words) after only a few weeks. Furthermore, their speech improvements transferred to words that were not trained during the therapy sessions. AMMT also yielded superior outcomes compared to CT, suggesting that the critical components of AMMT (intonation and bimanual activities) were likely to be responsible for the therapeutic effects. Results from our ongoing imaging study showed that the language-related regions and inter-regional connectivity of the brains of the nonverbal children are abnormal.

Conclusions: AMMT appears to have significant clinical potential in facilitating the development of speech children with ASD who are completely nonverbal. Its effectiveness may lie in its ability to engage and facilitate connections between language-related areas that may be abnormal in these children.

167.005 Methylphenidate Effects On Hyperactivity in ASD Are Moderated by Monoaminergic Gene Variants. J. T. McCracken^{*1}, M. G. Aman², L. Scahill³, L. E. Arnold², C. McDougle⁴, B. Vitiello⁵ and E. L. Nurmi⁶, (1)University of California, Los Angeles, (2)Ohio State University, (3)Yale University School of Medicine, (4)Indiana University School of Medicine, (5)National Institute of Mental Health, (6)UCLA Semel Institute

Background:

Methylphenidate (MPH) has benefit in reducing hyperactive-impulsive symptoms common in children with autism spectrum disorders (ASD), however individuals vary widely in response and tolerability.

Objectives:

We hypothesized that variants in key monoaminergic genes may moderate the clinical effects of MPH in ASD associated with hyperactivity and contribute to individual differences in their response.

Methods:

Sixty-six children ages 5 - 14 years (mean age 6.9 years) with DSM-IV Autistic Disorder,

Asperger's Disorder, and Pervasive Developmental Disorder Not Otherwise Specified (PDD-NOS) were randomized to varying sequences of placebo and three different doses of MPH during a 4-week blinded, crossover study. MPH doses used approximated 0.125, 0.25, and 0.5 mg/kg/dose twice daily with an additional afternoon half-doses. Primary outcome measures utilized include the Clinical Global Impression-Improvement (CGI-I) scale and the Aberrant Behavior Checklist (ABC-Hyperactivity Index). Subjects were genotyped for common functional and tag single nucleotide polymorphism (SNP) variants in the genes encoding the dopamine receptor subtypes 1-5 (*DRD1-DRD5*), the alpha adrenergic 2A receptor subtype (*ADRA2A*), the serotonin transporter protein (*SLC6A4*), and the enzymes monoamine oxidase A and B (*MAOA* and *MAOB*). Functional variants in the dopamine transporter (*SLC6A3*) and catechol-o-methyl-transferase (*COMT*) genes were also assayed.

Results:

MPH was associated with significant improvement on hyperactive-impulsive symptoms ($p < 0.001$), with 49% of the sample meeting responder criteria of CGI-I "much" or "very much improved" and a decrease of >25% of ABC-Hyperactivity subscale scores from baseline. Significant differences by *SLC6A4* STin2 ($p < 0.04$), *ADRA2A* rs1800544 ($p < 0.02$), *COMT* val/met ($p < 0.05$), *DRD1* rs5326 ($p = 0.007$) and rs 4867798 ($p < 0.05$), *DRD3* ser9gly ($p < 0.04$) and *DRD4* rs11246226 ($p < 0.05$) genotype were found for responders versus non-responders. Dimensional analyses of symptom severity for dose by genotype interaction showed associations with *DRD4* and *SLC6A4*.

Conclusions:

Individual differences in MPH's efficacy in reducing common ADHD symptoms in children with ASD may be moderated by genetic effects on dopaminergic and noradrenergic systems. Results are interpreted in relation to known expression and regulatory effects of associated variants and identified dopamine system differences in presynaptic dopamine uptake, DAT1 binding, and CSF HVA in ASD studies. Larger replication studies and tests of the clinical significance of the observed associations are warranted.

167.006 Psychotropic Drug Use and CAM in ASD: Prevalence and Correlates in the Ohsu ATN Site. K. Senn¹, J. B. Rouillet¹, L. Voltolina¹, D. A. Fair¹, A. D. Hagen¹, J. Nigg¹, L. Huang-Storms¹ and E. Fombonne*², (1)*Oregon Health & Science University*, (2)*Oregon Health and Sciences University*

Background: High rates of psychotropic drug use have been described in samples of ASD. An array of complementary alternative medicines is also commonly used in the management of children with ASD. Predictors of each approach have rarely been studied simultaneously in the same study.

Objectives: To investigate the prevalence of psychotropic drug use and use of complementary medicines (CAM) in ASD children, and to identify factors associated with their use.

Methods: Data were collected at the Oregon Health and Sciences University (OHSU) site of the Autism Treatment Network (ATN). Data on 426 ASD subjects (83.5% male; mean age: 5.4 years; range: 2.0 -16.9 years) were analyzed. Psychotropic drug and CAM use at diagnosis was recorded on a standardized form used for data collection through the ATN. Other data were available collected by professionals (diagnosis, autism severity, verbal level, cognitive assessments, Vineland Adaptive Behavior Scales) or parents (socio-demographic background, CBCL).

Results: The prevalence for any psychotropic drug was 32.6%, with 6.6% children on 2 or more drugs. For specific classes of drugs, figures were: 6.3% for amphetamine derivatives, 1.2% for atomoxetine, 3.5% for alpha2-adrenergic drugs, .7% for anticonvulsants, 2.6% for SSRIs, 3.1% for atypical neuroleptics, and 22.1% for melatonin. The prevalence of any CAM use was 27.9% in the entire sample, with figures of 2.3% for chiropractics, 2.3% for high dosing vitamin B6, 2.9% for essential fatty acids, 12.8% for other vitamin supplements, 9.6% for gluten-free diet, 6.3% for probiotics, 9.9% for casein free diet, 1.3% for digestive enzymes, 2.1% for no processed sugars, and 9.6% for other CAMs. 14.6% children were on 2 or more CAMs. Children taking psychotropic drugs were more likely ($p=.047$) to take CAMs as well.

Psychotropic drug use was unrelated to child gender, autism severity, verbal level, ethnicity, parental education, and adaptive functioning.

There was a strong relationship with age with psychotropic drug use rising continuously from 17.7% (under age 3) up to 60.5% (over age 10) ($p<.001$). Parent concerns about communication difficulties ($p=.03$), sleep problems ($p=.02$), aggressive behaviors ($p=.05$), hyperactivity ($p=.02$) and attentional difficulties ($p<.01$) predicted psychotropic drugs use. Other parental concerns (GI or neurological or eating problems, sensory issues, internalizing problems, social deficits, repetitive behaviors, SIB or loss of skills) did not.

For CAM use, differences of predictors were as follows. There was no age relationship ($p=.91$). Parental education was associated with CAM use ($p=.03$) with the lowest use (20.9%) amongst less educated. In contrast to psychotropic drugs, CAM use was strongly associated with high CBCL t-scores for anxiety ($p=.002$) and internalizing problems ($p=.02$) whereas all CBCL t-scores for disruptive behaviors (oppositional, aggressive, attention deficits) and the total scores were unrelated to it. CAM use was not related to sleep, language, disruptive behaviors parental concerns, but was uniquely associated with concerns for GI ($p=.001$) and anxiety ($p=.06$) problems.

Conclusions: Use of medicines is prevalent in the ASD population despite a weak knowledge base on their efficacy. Specific predictors for either psychotropic drug use or CAM use could be identified.

167.007 An Internet-Based Randomized Controlled Trial of Omega-3 Fatty Acids for Hyperactivity in Children with ASD. S. Bent¹, R. L. Hendren¹, T. Zandi², J. K. Law², F. Widjaja¹, J. E. Choi¹, J. Nestle² and P. A. Law*², (1)*University of California, San Francisco*, (2)*Kennedy Krieger Institute*

Background: Complementary and alternative medical (CAM) therapies, such as omega-3 fatty acids, digestive enzymes, and high-dose vitamins are widely used to treat ASD despite little or no evidence of efficacy and safety. Traditional, clinic-based randomized controlled trials (RCTs) of therapies for ASD are expensive and extremely slow, often taking several years and many millions of dollars to complete. We sought to evaluate one of the more promising CAM therapies, omega-3 fatty acids, with a novel, fully internet-based clinical trial methodology to both evaluate the efficacy of omega-3 fatty acids and determine if internet-based RCTs (IB-RCTs) in ASD are

feasible. Omega-3 fatty acids were selected because hyperactivity is a common problem among children with ASD and standard treatments (e.g., psychotropic medications) have unpredictable effects and more side effects in children with ASD. Two prior small pilot studies have found trends suggesting that omega-3 fatty acids may reduce hyperactivity in children with ASD.

Objectives: The goal of this study was to determine if the daily use of omega-3 fatty acids reduces hyperactivity compared to placebo in children with ASD and elevated baseline levels of hyperactivity. Secondary goals included assessments of change in social functioning, other ASD-related behaviors, and an evaluation of the performance of the IB-RCT.

Methods: This IB-RCT randomly assigned consented children ages 5-8 with ASD and elevated levels of hyperactivity to take 1.3 grams of omega-3 fatty acids daily vs. placebo over a 6-week period. The primary outcome measure was a comparison of the change in the hyperactivity subscale of the parent and teacher-administered Aberrant Behavior Checklist (ABC-H) between active and placebo groups. Secondary outcome measures included parent-completed Social Responsiveness Scales and Global Clinical Impression-Improvement scores. All study procedures, including recruitment, informed consent, assessment of inclusion and exclusion criteria, and collection of baseline and outcome measures took place over the internet. The diagnosis of ASD was established by parent report and by a threshold score on the Social Communication Questionnaire, a method which has been validated in earlier studies. This study was conducted using IAN's online tool, ORCA, which allows researchers to fully automate, track, and monitor complex protocols.

Results: The study opened for enrollment on September 18, 2012. As of October 9, 2012 (exactly three weeks into enrollment), 40 children from 22 U.S. states completed all enrollment procedures including engaging the child's teacher. After being randomized into the control group or the treatment group (double-blind), these 40 subjects are currently involved in different stages the trial. 54 additional families have completed informed consent and are currently involved in the

screening process. The trial and data analysis is targeted for completion by the end of 2012.

Conclusions: The IB-RCT method is a faster and less expensive clinical trial design than a conventional clinical trial design for the evaluation of many safe interventions. IB-RCTs can play a pivotal role in evaluating many commonly used, but unstudied interventions in ASD. Evidence from this study on the efficacy of omega-3 fatty acids will be available by end of 2012.

167.008 Extended Oxytocin Treatment of Children with Autistic Disorder. L. Sikich^{*1}, T. C. Bethea², C. O. Alderman³, L. Hazzard³, C. A. Pedersen⁴, N. E. Connelly³, S. G. Gregory⁵ and J. L. Johnson³, (1)*ASPIRE Research Program, UNC-CH*, (2)*University of North Carolina*, (3)*University of North Carolina at Chapel Hill*, (4)*University of North Carolina School of Medicine*, (5)*Duke University*

Background: Animal studies have demonstrated that oxytocin is important in regulating affiliative and nurturing behaviors in some species and that administration of a single dose of oxytocin to nonhuman primates enhances generosity and awareness of social hierarchies. Single doses of oxytocin in adults and adolescents with autism have been demonstrated to improve awareness of social behaviors and recognition of emotion. In adults with Fragile X, a single 24 IU dose of oxytocin improved eye contact. However, no clinical trials have yet examined the effects of repeated doses of oxytocin given for a sustained period of time in children with autism.

Objectives: Our aim was to determine if extended treatment with intranasal oxytocin would be tolerated by children with autism across the pediatric age range and to characterize any changes in social functioning associated with treatment.

Methods: We randomly assigned children ages 3 to 17 years with autistic disorder (DSM IV 299.0) confirmed by ADOS to 8 weeks of twice daily (AM and afternoon) treatment with flexibly dosed intranasal oxytocin or matched placebo.

Subsequently, all participants received twice daily oxytocin for 8 weeks. Participants were assessed with the Aberrant Behavior Checklist (ABC), the Social Reciprocity Scale (SRS), the Pervasive Developmental Behavior Inventory (PDD BI), the Vineland Adaptive Behavior Scales – 2

and Stanford-Binet. Adverse events were systematically elicited.

Results: 25 children, mean age 10.3 ± 4.4 (SD) years, were randomized: 12 to oxytocin and 13 to placebo. Eleven children were nonverbal and fourteen had fluent speech. Oxytocin was well tolerated with the exception of one participant who withdrew within 2 weeks of treatment with oxytocin due to worsening insomnia and agitation. Worsening oppositionality, aggression, irritability, poor concentration and gastrointestinal disorders were all more common during the course of placebo treatment than oxytocin treatment. Those treated with oxytocin showed reductions in many, but not all, measures of social functioning: ABC-Social Withdrawal $-2.0(1.0 \text{ SE})$ with oxytocin versus $-1.3(1.8)$ with placebo; PDD-BI Social Deficit Score $-2.8(1.6)$ with oxytocin versus $-1.5(2.0)$ with placebo; SRS Awareness $-4.4(2.9)$ with oxytocin versus $-2.1(3.9)$ with placebo, SRS Motivation $-5.8(3.9)$ with oxytocin versus $-2.1(3.5)$ with placebo, SRS total $-5.1(2.3)$ with oxytocin versus $-3.9(3.3)$ with placebo. They also had a significant reduction in ABC-Irritability: $-3.4(0.9)$ with oxytocin versus $-1.7(1.7)$ with placebo. Benefits continued to accrue during the 8 weeks of open oxytocin treatment.

Conclusions: Oxytocin was well tolerated by most children in the trial over 8 weeks of sustained treatment. It appeared to have benefit for reducing irritability and improving some aspects of social functioning. Larger scale trials of sustained intranasal oxytocin treatment in children with autism are needed to fully evaluate its safety and establish its efficacy for improving social functioning.

Cognition and Behavior Program

168 Cognition: Perception, Memory, & Emotion

168.001 Sex Differences in Dynamic Visual Scanning Patterns in School-Age Children with Autism Spectrum Disorders. J. M. Moriuchi^{*1}, A. Klin² and W. Jones², (1)*Emory University*, (2)*Marcus Autism Center, Children's Healthcare of Atlanta & Emory University School of Medicine*

Background: One of the most striking features of autism spectrum disorders (ASD) is the difference in prevalence based on sex. Due to the relatively low frequency of affected females, with a sex ratio of 4:1 (male:female) across the entire spectrum, many studies have excluded females or have

included sample sizes too small to detect potential sex differences. As a result, understanding of sex-specific differences in ASD-related social behaviors and how those differences may relate to the etiology of the disorder remains limited. Recent preliminary eye-tracking research with school-age children has suggested that although boys and girls with ASD do not differ in how much they look at others' eyes, the social adaptive value of looking at others' eyes *does* differ based on sex. The present study seeks to better understand how those differences emerge and how they are manifest in visual scanning patterns on a moment-by-moment basis.

Objectives: The aims of the current study were (1) to compare time-varying visual scanning patterns in females and males with ASD and (2) to investigate how time-varying visual scanning patterns are associated with an individual's level of social and cognitive functioning, both between sexes and within each sex.

Methods: Eye-tracking data were collected while 116 school-age children with ASD (81 boys, 35 girls) and 36 typically-developing peers (26 boys, 10 girls) viewed video scenes of children and adults engaged in naturalistic, age-appropriate social interaction within everyday settings. The ASD sample represented a broad range of level of social disability (ADOS Calibrated Severity Score: mean= $10.4(4.8)$, range=1-10) and cognitive functioning (Full-Scale IQ: mean= $95.4(21.5)$, range=42-149). Across diagnostic groups, both boys and girls were matched on age; within diagnostic groups, the sexes were matched based on age, IQ, and level of social disability.

Results: Results suggest that the time-varying visual scanning patterns of girls with ASD deviate from normative patterns less frequently than those of boys with ASD ($p < 0.001$). In addition, whereas the degree of deviation from normative scanning patterns is significantly associated with level of social disability in boys ($p = 0.004$), the relationship is not significant in girls ($p > 0.05$). Because the timing of deviations from normative visual scanning patterns largely overlapped between boys and girls, ongoing analyses are examining how visual attention during moments of deviation may differ between sexes and mediate the relationship with level of social disability.

Conclusions: The present study finds significant sex differences in how boys and girls with ASD engage with and learn from their natural social visual environment. These results not only suggest differences in developmental etiologies, but may also support targeted, sex-specific interventions.

168.002 Perception of the Sound Induced Flash Illusion in Adolescents with Autism Spectrum Disorders. J. K. Siemann*¹, R. A. Stevenson², B. C. Schneider³, H. E. Eberly³, T. Woynaroski¹, S. M. Camarata⁴ and M. T. Wallace¹, (1)Vanderbilt University, (2)Vanderbilt University Medical Center, (3)Vanderbilt Undergraduate Neuroscience Program, (4)Vanderbilt University Kennedy Center

Background:

Autism Spectrum Disorders (ASD) are complex neurodevelopmental disorders characterized by the presence of restricted or repetitive interests and impairments in communication and social or reciprocal behaviors. In addition to deficits in this triad of domains, there have been numerous reports of sensory deficits spanning multiple modalities in ASD. These reports have prompted investigations into better characterizing the nature and role of sensory and multisensory processing deficits in autism.

Objectives:

There has been a growing literature demonstrating atypical multisensory processing in individuals with ASD. One effective way of measuring multisensory integration is by using cross-modal illusions, such as the sound induced flash illusion (SIFI). In this illusion, when a single visual flash is presented in close temporal proximity to multiple auditory beeps, individuals often perceive multiple flashes. The basis of this illusion is the "binding" of the visual and auditory signals into a unified percept. The goals of the current study were to determine how ASD and typically-developing (TD) individuals perceive this illusion to probe for potential deficits in multisensory processing. Our hypotheses were that individuals with ASD would be less susceptible to this illusion due to deficits in multisensory binding processes, and that these differences would not be a consequence of changes in unisensory (i.e., visual alone, auditory alone) processing.

Methods:

32 TD individuals and 32 high functioning 6-18 year old individuals with ASD (2-subtest IQ: 115.7 (12.1) & 111.1 (16.1); $p > 0.05$) completed a sound induced flash illusion task where one visual flash was presented along with 0-4 auditory beeps. Control trials included 1-4 visual flashes presented with no auditory beeps. Participants were asked to ignore the beeps and report how many flashes they perceived. Individuals also completed unisensory auditory and visual temporal order judgment (TOJ) tasks in which they report which auditory or visual stimulus occurred first.

Results:

Perception of the illusion differed between groups. For illusory conditions, individuals with ASD were less likely to report multiple flashes than TD individuals ($p < 0.008$ for 2, 3 & 4 auditory beep conditions), suggesting a difference in the magnitude of multisensory binding. In contrast, there were no significant differences between groups for the control trials ($p > 0.2$ for 0 auditory beep conditions), or for performance on the unisensory auditory and visual TOJ tasks ($p > 0.05$).

Conclusions:

These results demonstrate that individuals with ASD perceive the sound induced flash illusion less often than TD individuals. This was not explained by differences in understanding or following directions or due to a bias to report a greater number of perceived flashes. This effect was specific to multisensory processing, since the unisensory tasks produced no significant differences. These preferential changes in multisensory processing for low-level visual and auditory stimuli suggest changes in neural networks responsible for multisensory binding in ASD. Furthermore, these results also suggest that deficits in early multisensory processes and networks may play an important contributory role in the higher-order domains known to be impacted in autism (e.g., communication, social interactions).

168.003 Spatial Transformations of Bodies and Objects in Adults with Autism Spectrum Condition. A. Pearson*, D. Ropar and A. Hamilton, *University of Nottingham*

Background:

Recent research suggests that individuals with autism spectrum condition (ASC) have particular difficulty in taking the visual perspective of others, that is, being able to say what a scene would look like from another person's point of view (Hamilton, Brindley, & Frith, 2009). Successful VPT depends on the ability to spatially transform a scene and the ability to consider what another person can see. Here we focus on the first of these, and examine the spatial processes which may underpin perspective taking in ASC.

Two types of spatial transformation are relevant. Egocentric transformations use the self as a reference frame, while mental rotation transforms an object independent of the self. There is little previous research into egocentric transformations in autism; however, research has shown mental rotation to appear unimpaired. Different classes of spatial transformations are often studied using different stimuli (bodies in egocentric transformations and objects in mental rotation), which makes it difficult to know whether effects are driven by group, task or stimulus.

Objectives:

The aim of this study is to understand the processes underlying visual perspective taking in autism. To examine this, we contrast egocentric transformations and mental rotation in typical and autistic adults.

Methods:

18 adults with autism spectrum condition and an IQ over 70, and 18 age and IQ matched typical adults took part in the study. Diagnosis of ASC was confirmed by ADOS. Each participant completed two reaction time tasks assessing their abilities to perform mental rotation and egocentric transformations on stimuli shaped like the human body or like a car. In the egocentric task, participants judged if the arm (of the body) or door (of the car) was extended on the left or right. In the mental rotation task, they judged if a body or car with one hand/door stretched out

matched an exemplar body or car. In each task, stimuli were presented at different orientations on each trial. Overall, this gave a 2x2x2x4 factorial design, comparing effects of task (egocentric and mental rotation), group (Autism and typical), stimulus (body or object) and stimulus orientation (4 levels).

Results:

Results showed that people with autism were slightly slower to perform mental rotation ($p=0.041$) compared to the typical participants, but no less accurate. However, in the egocentric task, participants with autism were significantly slower ($p<0.001$) and less accurate ($p=0.026$) than the typical participants.

Conclusions:

These data show that adults with autism may struggle with some of the basic processes underlying perspective taking. In particular, egocentric transformations are hard for this group, and were more impaired than mental rotation. Performance was not affected by the form of the stimuli (body or car). These data suggest that the fundamental process of relating a seen object to the self may be abnormal in participants with ASC.

168.004 Time-Based and Event-Based Prospective Memory in Autism Spectrum Disorder (ASD): The Roles of Theory of Mind, Executive Functioning, Time Perception, and "Future Thinking". D. M. Williams*¹, C. Jarrold², S. E. Lind¹ and J. Boucher³, (1)*Durham University*, (2)*University of Bristol*, (3)*City University London*

Background: Event-based "prospective memory" (EBPM) and time-based prospective memory (TBPM) involve remembering to carry out an intention upon the occurrence of a particular event or at a particular time-point, respectively. Everyday examples include remembering to turn off the bath taps before the bath overflows, remembering to pay a bill on time, or remembering to keep an appointment. It is clear that prospective memory is critical for flexible, independent living. To a greater or lesser extent, both forms of PM may rely on theory of mind, in that both require the retrieval of a previously-formed intention for success. The link between theory of mind and prospective memory may be

mediated by "episodic future thinking" (the ability to mentally project oneself through time to imagine future experiences of self).

Objectives: To assess the prospective memory profile and its cognitive correlates in ASD.

Methods: In Study 1, 21 high-functioning *children* with ASD and 21 age- and IQ-matched comparison participants completed TBPM and EBPM tasks, as well as background measures of executive functioning and theory of mind. In Study 2, novel EBPM and TBPM tasks, as well as measures of "episodic future thinking" and working memory, were completed by 17 *adults* with ASD and 17 age- and IQ-matched comparison participants.

Results: In Study 1, a significant Group (ASD/comparison) × PM task (Event-based/time-based) interaction, $F(1, 40) = 6.46, p = .02$, indicated that children with ASD showed significantly diminished TBPM, but non-significantly better EBPM than comparison participants. In Study 2, the interaction between Group and PM task observed in Study 1 was replicated exactly in this study, $F(1, 31) = 5.87, p = .02$, reflecting diminished TBPM, but unimpaired EBPM among individuals with ASD. In neither study was there any evidence that time perception contributed to diminished TBPM among individuals with ASD. There was evidence in Study 1 of a specific relation between diminished TBPM and diminished theory of mind.

Conclusions: These results provide clear (replicable) evidence for a specific profile of prospective memory ability/disability in ASD. Correlations between prospective memory task performance and background measures will be presented and the nature of cognitive underpinnings of prospective memory discussed. In particular, the issue of whether individuals with ASD employed compensatory strategies to perform well on EBPM tasks, despite limited/atypical underlying competence, will be addressed.

168.005 Recall of a Live and Personally Experienced Eyewitness Event by Adults with Autism Spectrum Disorder (ASD). K. L. Maras^{*1}, A. Memon², D. M. Bowler³ and A. Lambrechts³, (1)University of Bath, (2)Royal Holloway, University of London, (3)City University London

Background:

People with ASD may be over-represented in the Criminal Justice System, as a victim, witness, or perpetrator of a crime. Several studies have now explored eyewitness testimony in ASD (see Maras & Bowler, in press). None, however, have used a live eyewitness event in which the witness actively participated.

Typical individuals' memory is better for actions that are self-performed than actions observed being performed by another person. Several researchers have reported this "self-enactment effect" to be diminished or absent in ASD, however findings are inconsistent (see Lind, 2010).

Objectives:

To use a live eyewitness scenario to examine:

- 1) How well adults with ASD recall a participated-in eyewitness event.
- 2) Whether witnesses with ASD show a self-enactment effect
- 3) Whether they show impaired source monitoring for who performed which actions.

Methods:

Eighteen adults with ASD and 18 age- and IQ-matched (mean VIQ=110.86) comparisons participated in a live scripted eyewitness scenario whereby they assisted the experimenter perform first aid on a manikin-victim. There were 19 actions that the experimenter always performed and 19 that the participant always performed. One hour later participants provided their free recall (FR) account of this, before answering specific questions.

Results:

Groups did not differ in the number of correct details reported in both FR and questioning phases (all $F_s < .79, p_s > .38, \eta p^2_s < .02$), however the ASD group made significantly more errors

than their comparisons in both phases (all $F_s > 4.20$, $p_s < .05$, $\eta p^2_s > .11$).

There was a main effect of detail type for self-versus other-performed actions, $F(1,34) = 105.54$, $p < .001$, $\eta p^2 = .76$, but no group \times detail type interaction, $F(1,34) = 1.44$, $p = .24$, $\eta p^2 = .04$.

The ASD group made significantly more 'Self' source errors (incorrectly attributing self-performed actions as having been performed by the experimenter) than the comparison group in their FR, $F = 15.87$, $p < .001$, $\eta p^2 = .32$, but not questioning, $F(1,34) = .54$, $\eta p^2 = .02$. Groups did not differ in 'Other' errors in either phase, $F_s < .98$, $p_s > .33$, $\eta p^2_s < .03$.

Conclusions:

Overall findings indicate forensically that witnesses, victims or suspects with ASD may recall just as many correct details as their typical counterparts, but that investigators might seek to verify the veracity of details.

Both groups showed a self-enactment effect in both interview phases. Theoretically this indicates that individuals with ASD lay down a stronger memory trace for self-performed actions. Forensically it indicates that if an individual with ASD is involved in a crime they will be able to recall what they did.

The ASD group made more source confusions in FR (but not in questioning) in attributing actions that they had actually performed themselves as having been performed by the experimenter. Whilst ASD witnesses appear to lay down a stronger memory trace to recall more self-performed actions, they are also more likely to confuse their source. Difficulties in executive functioning (see Hill, 2004) might trigger pronoun reversal/confusion (e.g., Williams et al., 2011) in FR that, in line with the task support hypothesis (Bowler et al., 2004), are diminished with questioning. This has implications for forensic interviewing; witnesses with ASD may benefit from more specific direction in interviews to focus their recall.

Background: Individuals with Autism Spectrum Disorder (ASD) are often reported to have difficulty with emotion processing. However, clinical and experimental data show that individuals with ASD are sensitive to familiarity (e.g., they show normative attachment to familiar people), and they can share emotions with familiar others.

Objectives: Our aim in this study was to determine whether individuals with ASD would show normative physiological reactivity to the emotions of familiar people.

Methods: Participants were 25 young children with ASD and 22 young children with typical development, aged 2 to 5 years. The children observed videos of familiar people (therapists/child-care workers) and unfamiliar people expressing emotions (happy and fear), whilst their pupillary reactions were recorded using eye tracking technology. Visual attention (fixations) was also recorded to ensure children were looking at the emotional stimuli.

Results: Preliminary data analysis indicates that children in both groups differentiate between emotions and familiarity levels. The children with ASD showed a similar pattern of pupillary reactivity to the children with TD, but with one exception. The TD group, but not the ASD group, exhibited pupil dilation to unfamiliar people expressing fear. Although the children with ASD fixated less to emotions overall than the TD group, the pattern of fixations across stimuli was similar between groups.

Conclusions: As suggested by previous clinical and experimental findings, children with ASD react normatively to emotions of familiar people. Moreover, in responding to emotions, they appear to differentiate between familiar and unfamiliar people as do children with TD, but demonstrate hypo-reactivity to the expression of fear by unfamiliar people. These data have important research (i.e., use of unfamiliar people in emotional stimuli) and clinical implications.

Background: An atypical face and emotion processing in individuals with autism spectrum disorders (ASD) have received wide attention in the research of cognitive characteristics in ASD. Although many studies have tackled on this issue, it is still not clear whether / how their processing is different from typical people. In the current study, we focused on the "anger superiority effect". This effect refers a phenomenon where an angry face is detected more quickly than a happy or neutral face in a crowd of distracter. This is believed to be brought by the attention-getting properties in such threatening stimuli. Previous studies reported that individuals with ASD showed the quick anger detection ability as typically developed people did (Ashwin et al., 2006; Krysko & Rutherford, 2009). Interestingly, however, individuals with ASD showed weaker effect than the typical people at a larger crowd size. These previous findings raised a question, whether the rapid processing to the threat in adults with ASD is brought by the same mechanism as typical people use, or they use a different strategy to compensate their poorer emotion perception. In the latter case, the rapid processing to the threat in ASD can be considered to be acquired through their development. To address the question, we tested the angry superiority effect in children with and without ASD.

Objectives: In this study, we aimed to test the anger superiority effect in children with and without ASD, and to examine the developmental change in this effect.

Methods: 19 children with ASD ages 7 to 11 years old and 18 typically developing children (TD) with same age participated in this study. Visual search paradigm using touch-sensitive monitor was employed. Schematic facial stimuli including angry, happy, and neutral faces were used. The task includes two conditions to examine the search asymmetry effect. In the first condition, emotional faces were presented as targets and neutral faces were presented as distracters. In the other condition, neutral faces were presented as targets and emotional faces were presented as distracters. Participants were required to touch the object which is different from others as quick as possible. Reaction times in correct responses were measured.

Results: The results revealed that an angry face was detected more quickly than a happy face both in ASD and in TD. However, when integrating the effect of emotional stimuli both as a target and as distracters (Emotion Effect Index: EEI), which indicates the size of search asymmetry effect, the EEI was significantly different between the groups. Further analysis revealed that the EEI tended to be predicted by age in ASD, but not in TD.

Conclusions: These results suggested that children with ASD may acquire the sensitivity to the threat in faces as they grow up.

168.008 Perceptual Processing of Motion and Emotion in Low-Functioning Autism. B. HAN*¹, C. Tijus¹ and J. Nadel², (1)EA 4004 Lab CHArt/LUTIN, Paris-8 University, (2)CNRS USR 3246, Centre Emotion, La Salpêtrière hospital

Background: Whether persons with autism are affected by general visual peculiarities in movement processing or by selective peculiarities restricted to social stimuli is still a matter of debate. Recently, EEG responses to static emotional expressions tend to suggest abnormal cortical specialisation within social brain networks and increase activity of visual areas that disadvantage holistic facial processing. Meanwhile, visual areas are found to be normally sensitive to dynamic facial motion in typical and ASD groups. Put together, the above reported results stress the importance of a clear-cut distinction between processing emotion and processing motion.

Objectives: This study aimed at comparing in ASD and typical people the dynamical processing of physical, mechanical and biological stimuli and the scanning of regions of interests in human and robotic emotional expressions.

Methods: Twelve low-functioning adolescents with autism spectrum disorders (LFASD) diagnosed as such with DSMIV-R using ADI-R, 12 typically developing children (TD) matched on non-verbal developmental age, and 12 typical adolescents matched on chronological age (TA) participated in the study. The 36 participants were presented a novel morphing paradigm allowing a straightforward comparison of scores for dynamic changes in faces and in objects. The material was composed of 4 morphing videos of change of human emotional expression in face (happiness,

sadness, surprise, fear), 4 morphing videos of change of the same emotional expressions displayed by a mechanical set-up, and 4 morphing videos of change of state in graspable objects (a plastic bottle, scissors, a safety pen, a pencil case) presented at a speed of 4000 ms with 101 frames. Participants had to recognize the target image among non target images.

Results: Processing morphed stimuli, LFASD showed dissociation between performance for emotional expressions in faces and robotic set-up compared to graspable objects, while the TD and TA matched groups scored similarly for all three. Participants of each group were equipped with an eye-tracker in order to scan their exploration of the three kinds of stimuli. Here we focus on Regions of Interests (RoIs) and thus only include results concerning human versus robotic emotional expressions. For emotional faces, LFASD showed longer fixations to core emotional regions of interest (eyes and mouth) compared to the two typical groups. This however did not lead to a good performance in the processing of emotional faces. For robotic emotional patterns, ASD devoted significantly less attention to core emotional regions. Instead, they distributed equally their fixations between the two sources of motion: eyes and mouth on one hand and mechanical points on another hand. No such distribution was observed in the typical groups.

Conclusions: Results are discussed in terms of a possible use by individuals with autism of the same strategy for emotion and object processing which would lead to lower their performance when the dynamics of facial expression is concerned. Taken together, these results suggest a local processing of facial movement rather than a processing of emotional signals in ASD people.

Approaching Adulthood: Transitional and Vocational Issues

Chairs: D. Nicholas¹L. Zwaigenbaum² (1)*University of Calgary*, (2)*University of Alberta*

Aims (1) To identify gaps and opportunities for transitional and vocational research in ASD (2) To facilitate networking for research priority planning/development. Widespread un-/under-employment is reflected in low employment rates for persons with ASD. In a population-based ASD sample, fewer than half of participants were in paid employment or post-secondary education two years post-high school. Workplace and community barriers are reported. Evidence-informed transitional and vocational supports are lacking, with insufficient evidence guiding practice. To set the context, this SIG

session will comprise initial, brief literature syntheses by SIG team members outlining (i) ASD transitional/vocational literature gaps, and (ii) promising practices based on emerging evidence. Facilitated small group discussion will then target salient issues: transition preparation, vocational support resource development/testing, employer needs, and post-secondary education access/success. For each issue, the following questions will guide discussion (facilitated by a moderator, time-keeper and note-taker): (i) research priorities, (ii) steps for moving forward, (iii) strategies to engage stakeholders, and (iv) tasks for research mobilization beyond IMFAR. Lastly, reports back to the larger group will reflect each small group's discussion, including commitment/plans for further work. We will seek to include self-advocates and employers in the session and research in moving forward.

Autism Smig 2013

Moderators: A. E. Lane¹J. H. G. Williams² (1)*The Ohio State University*, (2)*University of Aberdeen*

The Autism SMIG (Sensory Motor Interest Group) will meet again at IMFAR 2013. The aims of this group are to facilitate information exchange and collaboration between researchers, and it is open to all researchers and others interested in sensory and motor aspects of autism. Also, we seek to educate the broader autism field about the latest findings in sensory and motor research and how these might be applied in practice. The Autism SMIG hosts a website, blog and Facebook page <https://www.facebook.com/ImfarSmig> for the purposes of communication throughout the year. At IMFAR 2013, we will conduct a "Data Blitz" along with focused discussions on early career mentoring and consensus terms for use in this area. For more information about the Autism SMIG website, please contact: lane.350@osu.edu. For more information about the Data Blitz, please contact: justin.williams@abdn.ac.uk. For more information about the Autism SMIG blog, please contact: j.cusack@abdn.ac.uk.

Autism Social, Ethical, and Legal Research

Chairs: E. Pellicano¹B. Siegel²M. Yudell³ (1)*Centre for Research in Autism & Education*, (2)*University of California, San Francisco*, (3)*N/A*

Recent scientific discoveries on autism have invoked a discourse of risk. Clinicians may talk about a child's "risk of developing autism." Scientists publish research describing environmental and/or genetic "risk factors" for developing autism. Educators speak of a child's "risk of a poor developmental outcome". And some members of the public believe that children who receive certain vaccines are "at risk of autism". The way stakeholders communicate such risk information – especially information that is probabilistic in nature – has enormous implications for autistic people, their families and for public understanding. How should we communicate "risk" information when the causes of autism or its developmental trajectory are not fully understood? And how should we tailor messages of risk to different stakeholders, including autistic individuals, parents, educators and practitioners and the broader public? In the second of a series of SIGs, we will discuss and debate the social, ethical and legal implications of issues surrounding risk communication. Speakers for the session include Simon Baron-Cohen, Professor of Developmental

Psychopathology, Autism Research Centre, University of Cambridge; Michael Yudell, Associate Professor and Director, Program in Public Health Ethics and History, Drexel University School of Public Health; Stephen Shore, Assistant Professor of Education, Adelphi University; Holly Tabor, Assistant Professor, Department of Pediatrics, Division of Bioethics, University of Washington School of Medicine; Martine Lappé, Institute for Society and Genetics, University of California, Los Angeles. This year we will work to pair junior and senior scientists interested in ethics and risk communication to work together as professionals and research mentors on these issues. We will also reserve twenty minutes during the session for junior scientists to offer brief presentations on their research in autism ethics and/or risk communication. If you are a junior scientist and are interested in presenting during this SIG, please send an email to myudell@drexel.edu.

Females With ASD

Moderators: A. M. Head¹W. Mandy² (1)*Deakin University, Melbourne, Australia,* (2)*Faculty of Brain Sciences, UCL*

This year's theme is "Defining the ASD Phenotype in Females". We will have a diverse panel of speakers who will each give brief (5 minute) talks outlining their particular view on how to move forward research on females with ASD. These short talks are designed to stimulate discussion: most of the session will be dedicated to group interaction and exchange of ideas. We believe that this will allow the members of the SIG to negotiate a consensus about the best way to move our understanding of the female ASD phenotype forward. Our aim is for the SIG to have a life that is not confined to the annual IMFAR meeting. To this end we have set up a new blog dedicated to the SIG which you can visit at <http://femaleasd.wordpress.com> We cordially invite people to read and comment on the blog, to foster independent connections and networks amongst people interested in understanding ASD in females. We will summarize SIG ideas from the 2013 IMFAR meeting and blog discussions in a review paper, setting out what is known about ASD in females, and outlining potentially fruitful strategies for future research.

Global SIG: Global Knowledge Translation for Research On Early Identification and Intervention in Autism

Chairs: M. Elsabbagh¹P. de Vries² (1)*Centre for Brain and Cognitive Development,* (2)*University of Cape Town*

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 initiate dialogue, 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 "Lost in translation: Scientifically valid and contextually appropriate use of early screening and diagnostic instruments".

Minimally Verbal Individuals

Moderators: N. Jones¹T. Katz²C. Kasari³ (1)*Autism Speaks,* (2)*University of Colorado Denver,* (3)*University of California Los Angeles*

An estimated 30-40% of school-aged children with autism spectrum disorders (ASD) remain minimally verbal even after receiving years of interventions. Very little is known about individuals at this end of the autism spectrum partly because this is a highly variable population with no single set of defining characteristics, and partly because these individuals are excluded from most research studies. This SIG aims to promote research that will help characterize children with ASD who are nonverbal/minimally verbal and forge collaborations among researchers interested in developing new assessments and effective interventions. We will use our first meeting to establish working groups of investigators at various levels of experience and training to develop priorities for new research programs. The goal is for workgroups to establish ongoing collaborations that will be reviewed at subsequent IMFAR meetings. Our SIG will have an initial focus on: characteristics of children with ASD who are minimally verbal, assessment methods of these children's abilities and skills, evaluation of co-occurring physical and psychiatric conditions, and effective interventions including augmentative supports.

Relationship Between Criminal Justice Policy and ASDs

Moderator: L. A. Sperry *Griffith University/University of Sunshine Coast Australia*

This SIG will begin with an interactive panel discussion which examines criminal justice systems, the characteristics and life circumstances of people with ASD that are implicated in criminal behavior, criminal responsibility and culpability. The prevalence of people with ASD who engage in criminal behavior relative to their prevalence in general society is difficult to determine with precision. Attempts to aggregate prevalence data are compromised by the individual differences that exist in data keeping globally, the validity of diagnoses, and the accuracy of reported offenses. This area of autism research and clinical practice has significant implications for improving outcomes for individuals with ASD who are coming in contact with the criminal justice system. Subgroups within Criminal Justice Policy will be formed to further the discussion and reflect the individual interests of attendees (e.g., risk factors vs. policy vs. treatment) as well as provide essential networking and mentorship opportunities. We look forward to initiating a global dialogue regarding the scope of this issue and what we, as scholars and clinicians, can do to inform intervention, treatment and improve criminal justice policy and practice.

Technology and Autism: Developing a Framework for Best Practice in Design, Development, Evaluation and Dissemination of Autism-Specific Technologies.

Moderator: S. Fletcher-Watson *University of Edinburgh*

People with autism are significant consumers of technology, which is often beneficial. Despite the proliferation of autism-specific technologies, as embodied in the IMFAR Tech Demo, there is no agreed theoretical foundation, no consistent methodology for design or evaluation, and a lack of evidence base to inform consumer choices. The goal of this cross-disciplinary and international SIG is to create a model for best practice in the field, addressing issues raised at a recent event [5], including: • Theoretical models for technology development and implementation • Creating autism-specific features of technology,

using participatory design • Evaluating hardware and software and supporting access to those which are demonstrably beneficial • Guiding families and practitioners in technology selection Outcomes will include publication of a series of papers as a journal special issue and a free-to-download booklet offering guidance to practitioners and parents. These issues are pressing in the light of concerns about screen time for young children [6] and the rapid rate of development of commercial technologies. In future years, the remit of the SIG could be extended to consider the ways in which technology can be harnessed to provide autism support in developing nations, and to support autism across the lifespan.